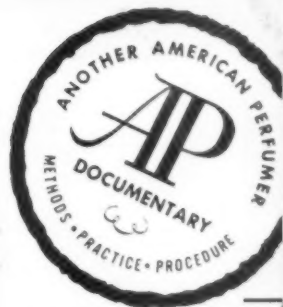


American Perfumer

AND AROMATICS



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MAY 1959

THE MAGAZINE OF TASTE AND SCENT



12

Articles on Cosmetic Products Formulated
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American Perfumer AND AROMATICS

VOL. 73, NO. 5

MAY 1959

Contents

PHARMACEUTICAL COSMETICS

Introduction	Maison G. deNavarre	20
Transdermine		21
Possible Use of Anticholinergic Drugs as Antiperspirants in Cosmetology	Robert Brun, Ph.D.	22
Topical Steroids in Ageing and Senile Skin Cosmetics		24
Glycyrrhetic Acid, A Rational Use of	F. Quentin Evans	28
Neomycin in Deodorant Preparations	H. A. Nelson	33
Acne with Cosmetic Preparations, The Treatment of	Irwin J. Lubowe, Ph.D.	35
Allantoin		37
Sulfur in Cosmetics and Dermato-Therapeutics	T. E. Neesby	38
Are Topical Vitamins Underestimated?	Barclay Newman and B. T. Palermo	44
Topical Chemical Antiinfectives	Dr. Emil Klarmann	48
Vitamins in Cosmetics E. De Ritter, L. Magid, and P. E. Sleezer		54
Estrogens and Other Hormones, The Use of		59
A Contribution to the Study of Some Organ Extracts	Dr. Jean M. Cotte	60

DEPARTMENTS

News	9, 74	Technical Abstracts	66
Desiderata	15	Packaging and Promotion ..	72
Questions and Answers	64	Index to Advertisers	86

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May, 1959

Gathering Momentum

Time there was, not too long ago, when a sharp line could be drawn between what was distinctly a cosmetic manufacturer on the one hand and what was strictly a pharmaceutical firm on the other. Not so today. Some manufacturers almost imperceptibly drifted into each other's field without any formal announcement or fanfare. Rather, it was the character and nature of new products coming off the production line that brought about an awareness that a change had been taking place.

On the opposite side, of course, we have recently witnessed the prominent entry of Revlon into the pharmaceutical field. And just the other day big news was made by Colgate-Palmolive's announcement of its entrance into the drug field.

With this overlap of cosmetic-pharmaceutical products, comes wider opportunity for those who are engaged in research and laboratory work. Certainly, the cosmetic and the pharmaceutical chemists have much more in common today and can gain from each other's experience and know-how.

Elsewhere in this issue is the fourth, and perhaps the most timely, of our Documentary series: "PHARMACEUTICAL COSMETICS."

Much could be said here to extol the scope and merit of "PHARMACEUTICAL COSMETICS," not to mention the eminence of the talented contributors who made this Documentary possible. But we firmly believe that this feature will speak for itself.

The Colgate-Palmolive news also brings to mind some recent comments we were pleased to receive from Colgate-Palmolive people in regard to our Documentaries. "I do think their publication in this form serves a very useful purpose". Another had this to say: "Cosmetic Emulsion I thought excellent". From a recently acquired division of Colgate-Palmolive: "I think this series is wonderful." And finally, "I hope to see more of this type of material . . . a most valuable reference."

This issue also includes another example of editorial enterprise. We have reference to the sixteen abstracts which appear on pages 66 and 67. The important papers, abstracted only, were delivered on April 15, 16, and 17th at the British Congress of Cosmetic Science, London.

James H. Moore, Jr.
Publisher

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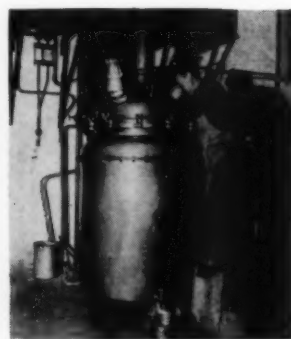


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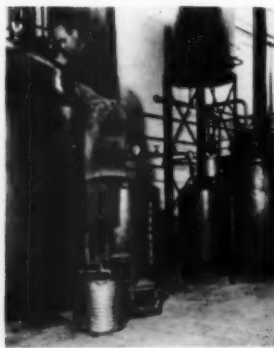
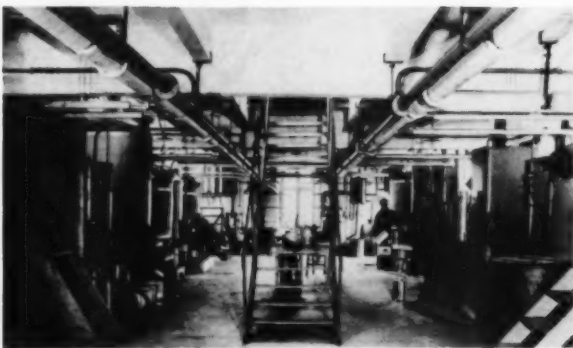
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May, 1959



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MINUTE NEWS . . .

Smith Kline & French Creates Medical Fellowship

The creation of the Smith Kline & French Fellowship in physical medicine and rehabilitation for a Mexican physician to undertake post-graduate training in the U.S. was announced simultaneously in Mexico City, by Ambassador Robert C. Hill and Mr. Romulo O'Farrill, President of the Mexican Rehabilitation Association, and in New York by Dr. Howard A. Rusk, President of the World Rehabilitation Fund, Inc. The fellowship will provide a three-year period of training in physical medicine and rehabilitation for a physician from Mexico. Dr. Leobardo Ruiz of Mexico City has been selected as the first recipient of the fellowship, which was made possible by a contribution of the Smith Kline & French Foundation.

International Symposium On Aerosols Planned

The first international symposium on aerosols will take place in Paris on June 26. The symposium, organized by the French Committee on Aerosols, is the first activity of the new European Federation of Aerosol Associations. Information about the symposium can be obtained by writing to the Comité Français des Aerosols, 51, Rue Boursault, 51, Paris (17^e), France.

Yardley Opens New Research Division

Yardley and Co., Ltd. is adding a new research division, to be known as Yardley International Research Laboratories, to its world-wide organization. T. Lyddon Gardner, managing director, has announced from London. The new division will be located in Union City, New Jersey. Sabbat J. Strianse, a past president of the American Society of Cosmetic Chemists, has been appointed director of research. The function of the Laboratories will be the exploration of new concepts in cosmetic chemistry and their practical application to product development.

Canco Earnings Up 10 Per Cent

American Can Company reports record sales for the first quarter of 1959, with earnings 10 percent higher than a year ago. Sales for this period amounted to \$227,084,796, the highest in the firm's history.

Toilet Goods Sales Up For 1958

The annual estimate of The Toilet Goods Association of retail business in perfumes, cosmetics, and other toilet preparations, excluding toilet soaps, for the year 1958 amounts to \$1,523,700,000. This is an increase of almost exactly 6.5 per cent over the previous record level set in 1957. The increase was spread quite generally over the entire range of toilet preparations.

Lanolin Plus Launches New Product

The biggest advertising campaign in Lanolin Plus history for its newly acquired product Rybutol, recently purchased from the Rexall Drug Company, started on May 1. The Company plans to spend approximately one million dollars during a three-month period in a drive to recapture a sizable chunk of the vitamin market.

Pharmaceutical Uses For Aerosols

Use of inhalation aerosols in the detection of lung cancer, in the application of insulin and other diabetic drugs, as a new way to administer "mood elevators" and as a replacement for the hypodermic syringe in taking serums represent important new areas for research, Samul B. Prussing, vice-president of Aerosol Techniques, told members of the Canadian Pharmaceutical Manufacturers Association at their meetings in Windsor, Ont. Mr. Prussen stated that today the application of inhalation aerosols in the administration of "miracle drugs" compares to the frontiers established with the development of the hypodermic needle and syringe.

Jean Crabalona Receives Degree

Jean Crabalona, of Laboratories R.E.A.C., Grasse, France, has been awarded a Doctorate in Science by the University of Lyon. His thesis on "the application of the Prince reaction in monocyclic terpenic series" won him *cum laude* honors. Dr. Crabalona is the son of Laurent Crabalona, Director of Laboratories R.E.A.C.

Justin Dart To Receive Honorary Degree

The New England College of Pharmacy will award an honorary Doctor of Science degree to Justin W. Dart, President of Rexall Drug Company at the New England Mutual Hall, Boston, on June 7. Mr. Dart will also deliver the commencement address.

Lehn and Fink Celebrates 85th Birthday

The 85th anniversary of Lehn and Fink Products Corp. was celebrated at a meeting of the company's Quarter Century Club on May 1 at the Waldorf-Astoria, New York. Dr. Edward Plaut, president of the company, was presented a gift by his employees, commemorating the 85th birthday. Special guests at the Club's sixth annual meeting were Francois Goby, president of Tombarel Freres of Paris and his brother Jean Goby, general technical director. New officers of the Quarter Century Club were installed. They include Henry Pollitzer, president; Mrs. Laura Ruth Birckholtz, vice president, and Miss Harriet Dean, secretary.

Chemical Specialties Manufacturers Meet

The Chemical Specialties Manufacturers Association holds its 45th midyear meeting on May 18-20 at the Drake Hotel, Chicago. Among the guest speakers were William C. Stolk, President of the American Can Company; James Q. du Pont of E. I. du Pont de Nemours & Company; Jame K. Langum of Business Economics, Inc. and Larry Le Sueur, CBS news analyst.

Industry People

Murray Stempel is the new president of Morningstar-Paisley, Inc. George J. Muller, previous president, vice-chairman of the board. . . . Clifford Pettitt is new general sales manager at Warner-Lambert with full responsibility for sales of all Hudnut-DuBarry products. Gilbert Klein named assistant to the president, and Irving Mettelmann promoted to manager of department and drug store sales. . . . Donald E. Clarke appointed personnel director of Max Factor & Co. . . . Heinz Eiermann and Robert Goldemberg named associate directors of toiletries research at Shulton, Inc. . . . Edward A. Ochs is new marketing vice-president of Hazel Bishop, Inc. . . . Wallace T. Drew appointed vice-president in charge of marketing at Coty, Inc. Lester J. Koeppen is new vice-president in charge of sales, and Morgan D. Lefjerdink is vice-president in charge of the wholesale division. Jean P. Millon is new vice-president in charge of trade relations.

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CHENAMBROL Soluble product of extraction of Mousse de Chene and Ciste. Available also decolorized.

DISTIRIS Reconstitution from fractions of natural oils other than Iris Butter, distilled over Iris Roots.

DISTIRONE Reconstitution of Absolute Iris (Irone) odor in a mixture subsequently distilled over Orris Roots.

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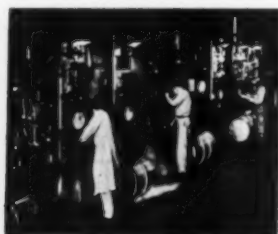
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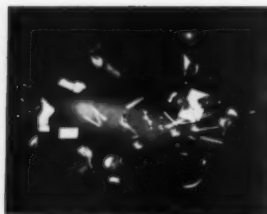
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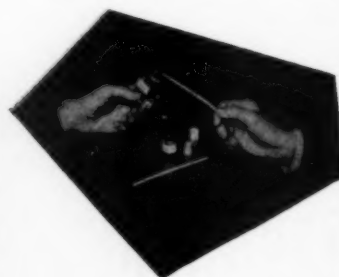
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Cosmetic Research



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Creative Perfumer



Perfume
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DESIDERATA

Maison G. deNavarre, M.S., F.A.I.C.



PVP HAIR SPRAY PATENT

We have already published a note on the issuance of U. S. Patent No. 2,871,161, on January 27, 1959, covering "sprayable water-free alcoholic PVP hair preparations," applied for on July 31, 1952, in the name of Maurice Spiegel of La Maur, Inc., Minneapolis, Minnesota. Mr. Spiegel has sent us a form letter as well as a formal one. We quote from them:

"Several years ago, our firm, La Maur, Inc., created an innovation for the cosmetic industry by inventing and developing a non-sticky, non-cracking, water-soluble film for casting onto the coiffure by spray application, which we package and sell under our trade-mark 'STYLE.'

"The United States Patent Office has now recognized our contribution to the art as being meritorious, and has granted to us a patent for our invention. Since the essential element of our invention is a water free alcoholic solution of polymerized units of the N-vinylpyrrolidone monomers, our patent encompasses both polyvinylpyrrolidone itself as well as its co-polymers.

"Although we have obtained exclusive patent rights on our invention, we have no desire to be selfish about such rights. It is our plan to offer other reputable firms in the field the right to share in the use of our invention, through appropriate licenses to practice it.

"Because the task of loading aerosol containers is a specialized field, conducted principally by a limited number of reputable firms, it is our belief that we should confine our licensing program to direct dealing

with such specialized firms, as well as the relatively few large cosmetic manufacturers who perform their own loading operations.

"If you are presently engaged in the loading of aerosol hair sprays of the composition indicated by the claims of our patent or if you contemplate entering this field of activity, we suggest that you inquire

British Congress

A historic meeting took place in the rooms of the Chemical Society, Burlington House, on April 15th, 1959, when representatives of eight countries met to discuss the formation of an International Federation of Societies of Cosmetic Chemists. This Federation would link together the various autonomous national bodies into an international body, capable of acting in such fields as International Standards, establishment of the professional status of the cosmetic scientist, publication of bulletins, abstracts and reviews on cosmetic science, to name only a few.

The countries represented on this occasion were: Belgium, Denmark, France, Germany, Great Britain, Norway, Sweden, and the United States. Agreement was reached on a provisional constitution. The delegates are now returning to their national Societies and as soon as possible a second Council meeting will be held to draw up a final Constitution. A provisional secretariat has been established in London, but the final headquarters remains to be agreed.

about our proposed licensing program. We intend to take full advantage of our patent rights against any infringers who do not become licensees."

ANTIBIOTICS IN COSMETICS

The case for antibiotics in deodorants is well put in another place in this issue by Harrison A. Nelson. But in the April 4, 1959, issue of the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Nelson and Sulzberger put the case against the use of antibiotics in cosmetics excepting possibly in deodorants.

They call attention to the hazard of sensitivity to neomycin, for example.

They also stress potential harm from possible absorption.

All this is good.

(But this writer wishes medical practitioners would pay heed to this, for their rather easy manner in prescribing antibiotics for simple ailments is known to all. Indeed, the readiness with which more sensitizing antibiotics are used in medical practices is enough to make your hair turn gray.)

I think both Nelson and Sulzberger have done a pretty fair appraisal of the situation in this article. Don't let the cautions stop with cosmetic practice. Furthermore, it is doubtful if there is such a thing as will "not produce toxic effects of any sort" with all people in the normal course of living. Wish there was.

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Emulsifiers

For ease of use — For dependable results —
For solving difficult problems

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Glyceryl Monostearate — Acid Emulsifying. For anti-perspirant — deodorant creams, lotions and ointments — all greaseless, medicated formulations.

Tegin...

Glyceryl Monostearate — Self Emulsifying. For neutral greaseless creams, lotions, ointments, suntan creams.

Tegin 515...

Glyceryl Monostearate — Non Self-Emulsifying. Used in conjunction with auxiliary emulsifiers.

Tegin P...

Propylene Glycol Monostearate — Self Emulsifying. For greaseless creams — brushless shave, foundation, suntan: lotions — foundation, suntan, ointments.

Lanolin Absorption Bases

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Mineral oil	10
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Borax	0.5
Water, Color, Perfume and Preservative, q.s.	100
*Dimethyl polysiloxane	

Adapted from a silicone manufacturer's literature, the directions call for putting "everything into the pot," heating up to 165-170°F., mix rapidly to a temperature of 120°F., perfume, color and package.

PERMANENT WAVE PATENTS

An important and interesting exchange of "Letters to the Editor" has taken place in **CHEMISTRY AND INDUSTRY** (page 145 and 322, 1959) between H. N. Walker, formerly of the Australian Patent Office and an anonymous patent agent.

Walker has referred to the Maeder Busch patents and said that it has been practically impossible to get a permanent wave patent, including one on thioglycolates because of this case, in Australia.

The anonymous patent agent brings up the subject in another way—suggest that if you are permanent wave conscious—read the original.

NOTES

Though Royal Jelly has lost its rocketing rise in excitement, the Queen Bee has not—now it's fresh from France, a Queen Bee Wax for hair removal. . . . Also from France, amniotic liquid for cosmetics, rich in hormones, biostimulins, certain vitamins, simple and complex proteins, amino acids, etc. . . . Marcussen (*Brit. J. Dermatology*, March, 1959, p. 97) points up the growing incidence to nickel sensitivity. In 1931 it was eighth in frequency and in 1955 it was third. (It is said to be second to only *p-phenylenediamine*). Continued inflation will probably make the 5 cent coin, the "nickel," disappear, but until then there is a problem worth watching. . . . Congratulations to Steve Mayham and TGA on the confidential study recently made on lipstick colors. All members got a copy of this bulletin. Nonmembers are out of luck, but can get it if they join up. . . .

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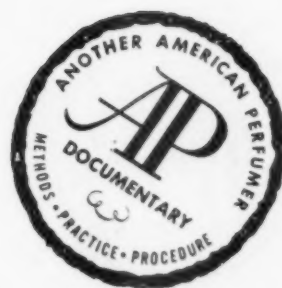
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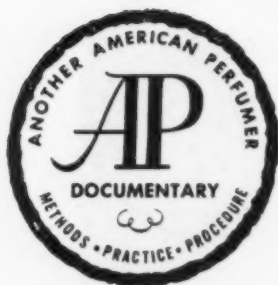
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PHARMACEUTICAL COSMETICS

The sharp line between pharmaceuticals and cosmetics has been dimmed by the emergence in recent years of dermato-cosmetic formulations and products. What follows is another AMERICAN PERFUMER & AROMATICS' documentary, covering this new and important development.



PHARMACEUTICAL COSMETICS*



Maison G. deNavarre, M.S., F.A.I.C.

With my training in pharmacy, I have always felt a close kinship between cosmetics and pharmaceuticals. Indeed, cosmetics may easily be classified as elegant, nontherapeutic pharmaceuticals. Galen's cerate, reputed to be the forerunner of cosmetic "cold" creams is in its elaborated form a pharmaceutical cosmetic.

Some years ago it became apparent that the "non-therapeutic" adjective describing cosmetics would have to be dropped. The new Food Drug and Cosmetic Act had redefined cosmetics. We then found cosmetics sold for years as such, suddenly became drug-cosmetics.

Antiperspirants were the first to be reclassified. Today they are joined by hormone preparations, acne and dandruff cosmetics, to name some. If Royal Jelly, Placenta and other organ extracts, phytohormones and related substances possess any demonstrable therapeutic activity, affecting an organ of the body, they too will come into this category.

More recently, there has been a trend toward more therapeutically active cosmetics. A recent introduction of an estrogen-progesterone cosmetic cream, is an indicator of the thinking now found among cosmetic scientists. Then too there is malonic acid, used to inhibit enzymes which influence the flow of perspiration.

Antibiotics have found their way into cosmetics. The corticosteroids, had they not been shown to be absorbed in appreciable amounts, would have become "over-the-counter" and would have undoubtedly found their way into cosmetics. Indeed, the corticosteroid creams and lotions sold on prescription are elegant products, which could easily qualify as cosmetics from the point of view of appearance, texture and odor.

Enter the aglycone of glycyrrhinic acid, the sweet principle of licorice, a nonsteroidal anti-inflammatory agent, glycyrrhetic acid.

We could not do a story on this any better than the one being reprinted from a British medical journal over the signature of a qualified dermatologist, F. Quentin Evans. It struck us as being quite inclusive—sufficiently to interest more people on this side of the Atlantic.

The anticholinergic drugs have often been studied for

their effect on antiperspiration. Dr. R. Brun summarizes present knowledge, including some of his own original work.

Antiperspirancy is completed with a bit by Harrison A. Nelson on the potential usefulness of Neomycin as a deodorant in such products.

Then there are the skin germicides. Pharmaceuticals? Yes. Cosmetics? Why not? Skin hygiene is a cosmetic practice. To get a kaleidoscopic view of this wide field, we were fortunate to get a many-times contributor to the *American Perfumer*, Dr. E. G. Klarmann who needs no introduction to anyone connected with this field as well as cosmetics, to cover dermatologically useful antiseptics.

Sulfur has "come-back." Dr. T. E. Neesby, an author on this subject of considerable reputation has given us a general review of this field and what can be expected from the particular source of sulfur used.

Like us or hate us, we had to cover the external use of vitamins, particularly for their local effect. A former fellow Detroiter, same alma mater and professional fraternity as this writer, capable Blaise Palermo, has brought this subject up to date.

Then there is another rediscovered substance, allantoin and the more recent allantoinate. S. B. Mecca, inventor of the aluminum allantoinates tells us about these new dermatological agents.

An expert on the subject, Dr. Max A. Goldzieher has answered important questions on hormones and their skin effect.

A diplomate of the American Board of Dermatology, Dr. Irwin I. Lubowe is writing on the cosmetic aspects of acne, a subject with which he is well acquainted.

To this we have added a digest of two patents, the subject of which shows the direction of thinking in conjunction with geriatric cosmetics.

Finally, it should be said that all this has been precipitated by the new influence of cosmetics on pharmaceuticals. Products for therapeutic use are now formulated from the aesthetic point of view as well as for the therapeutic result.

All in all, pharmaceutical cosmetics are on the doorstep. Examine them well.—M. G. deNavarre

* The opinions expressed in the foregoing articles are those of the respective authors and not necessarily those of the Moore Publishing Company, Inc.

TRANSDERMINE

A new synthetic lecithin-like material containing all the chemical entities found in the natural product has recently been introduced under the name of Transdermine.



A new synthetic lecithin-like material containing all the chemical entities found in the natural product has recently been introduced under the name of Transdermine. It contains glycol esters of fatty acids, a phosphate radical, an amino alcohol and the material is substantially free of unsaturates.

Transdermine is composed of two fractions—a solid base and a liquid portion. The commercially manufactured product is a uniform blend of these two fractions. Transdermine, in whole, is a wax-like material, ivory to white in color, melting range 52°-58° C. It is insoluble in the usual solvents such as ethyl alcohol, acetone and glycerine. It is slightly soluble in petroleum benzine, ether and mineral oil. It is soluble in chloroform and carbon tetrachloride. Some of its approximate constants range as follows:

Acid value	90±5
Ester value	134±5
Saponification value	224±6
Iodine	4
Odor—Almost odorless to very slightly aromatic	
Ash—Minimal	

So much for its characteristics. What is it good for?

Well, it derived its name from the fact that it is an excellent vehicle for transporting therapeutically active substances through the skin. It is aimed at getting quick therapeutic results. In doing so, it is apparently not completely metabolized. It either returns to the skin or resides there all the time.

In one experiment (3) this material was compared to lanolin and petrolatum as vehicles for 28 different medicinal agents. In general, it took twice as much of the medicinal agents when lanolin and petrolatum were the vehicles as compared to this synthetic, lecithin-like material. Imagine the savings in cost and the margin of safety capable of resulting from the use of this base.

Sternberg has published results on absorption using radioactive substances such as I^{131} and P^{32} (1). Other publications on the use of this substance as a drug vehicle have also appeared (2, 3).

Basic Cream Vehicle

This new lecithin-like material is readily mixed with other ingredients. It easily forms stable emulsions with water buffered to pH of 4.0 to 4.5 for maximum stability. The following base formula has been suggested by the manufacturer:

13.5	Transdermine
13.5	Vegetable Oil, Preserved (Sesame Oil)
72.85	Distilled or Deionized Water
0.15	Preservative Methyl Paraben—0.12
	Propyl Paraben—0.03

q.s. Lactic Acid
q.s. Perfume
q.s. Sodium Lauryl Sulfate
q.s. Other Special Ingredients

Heat transdermine, vegetable oil and preservative to about 70° C., until liquefied. Add the distilled or deionized water previously heated to about 75° C. Mix well and add sufficient lactic acid to bring the pH to 4.0-4.5. Continue the agitation until the temperature of the cream drops to about 45° C. Add the perfume and mix well. Allow the creams to stand for 24-48 hours before packaging to permit creams to set.

Note: The addition of lactic acid sufficient to bring the pH of the cream to 4.0-4.5 is necessary to bring about the cream consistency and provide greater stability to the cream. The further addition of 0.5 to 1.0% of sodium lauryl sulfate will often improve the stability of the cream where difficulty is encountered because of the presence of some additional ingredients or variations in manufacturing procedure.

Dermatopharmaceutical Uses

As a carrier for any therapeutic agent intended for local effect, this base may enable you to reduce the amount of active substance required with the associated lowering of cost and incompatibilities.

General Therapy

It appears that other than locally active therapeutic agents can be used for a systemic effect by bringing more of the active drug into the circulation. Steroidal hormones are a case in point.

Cosmetic Uses

Besides serving as a valuable vehicle for medicinal agents, the base cream itself is a useful cosmetic product.

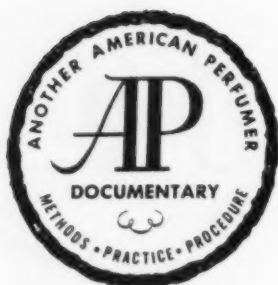
Whenever penetration is desired, this vehicle should serve well. Thus, antiperspirants, dermatotherapeutic agents, dandruff products, skin stimulation creams and lotions and antiseptic applications are a few of the potential uses.

Conclusion

A new base with great potential use in drugs and cosmetics is now available in pilot plant production. Work on its adaptation to particular uses promises interesting results. Experimentation with this product is recommended to all progressive research departments.

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Possible Use of Anticholinergic Drugs as Antiperspirants in Cosmetics

It is well known that sweat delivery is stopped by the inhibition of the peripheral nervous system. Here is a study of the use of some oral drugs and their antiperspirant effect.

BY ROBERT BRUN PH.D.*

What about the possible uses in cosmetics, of antiperspirants acting through the medium of the neurovegetative system, that is to say of products having an atrophinellike action? It is indeed well known that sweat delivery is stopped by the inhibition of the peripheral nervous system.

Introduction

When substances such as pilocarpine, acetylcholine and so on are inserted in the skin (for instance by intradermic injection or by iontophoresis) the sweat glands of the region touched by the drug act nearly immediately. The pharmacologists know the products of this category well and have labeled them "parasympathomimetics" or according to some "cholinergics." If before the experiment is carried out, another substance of the atropine or scopolamine type is inserted in the selected region of the skin, perspiration will not be induced. This because the second type of substance is an antagonist to the first one. These second substances have been named

"parasympatholytics" or "anticholinergics." These experiments added to other ones show that the eccrine sweat glands are innervated by nervous fibers of cholinergic type. A very good survey of the problem can be found in Rothman's Physiology and Biochemistry of the skin.

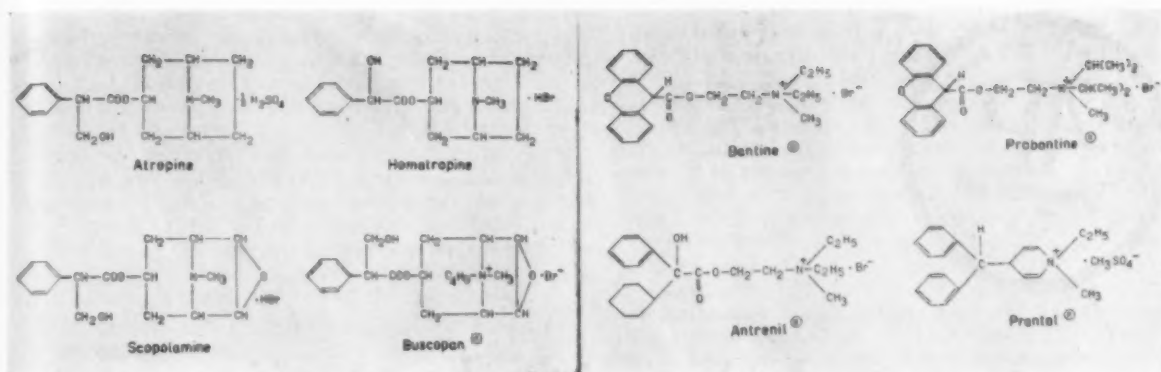
The Anticholinergics or Parasympatholytics

For a long time the principal representatives of the group were the natural alkaloids of *Atropa belladonna* and *Hyoscyamus niger* i.e. atropine and scopolamine. During these last years numerous synthetic products with an anticholinergic action appeared on the market. The principal indication of these new drugs is for gastric ulcer, indication set specially on the ground of the inhibitive effect on the gastric secretion. It was noticed that most of these products given in a certain quantity also brought on a dryness of mouth and eyes, as well as a decrease of perspiration. This last fact induced the manufacturers of these anticholinergic drugs to advise them equally to combat hyperhidrosis. As a reminder, the products of this group dispensed by iontophoresis do not only inhibit the sudoral secretion induced by pilocarpine, etc. but also the perspiration due to heat as Shelley and Horvath demonstrated it.¹

The Human Sweat Gland as Test Organ in Pharmacology

Most pharmacological tests enabling us to set forward the cholinergic or anticholinergic effect of a product are carried out on animals. Besides the secretory or anti-secretory activity of these drugs on the human sweat gland is little or not examined. In the Dermatological Clinic of Geneva, we have undertaken a series of studies to complete our knowledge in that sphere. A summary of the techniques used for these experiments as well as the corresponding bibliography was recently published in the U.S.A.² Our studies brought us to examine the duration of the effect and the antisecretory activity (rela-

*Department of Dermatology of the Geneva University Hospital (Prof. W. Jadassohn, Chairman), Geneva, Switzerland.



tive to pilocarpine) of diverse anticholinergic drugs locally dispensed by iontophoresis.² The results obtained were subsequent:

Substance	Dose	Sweating induced by pilocarpine		
		total inhibition	partial inhibition	no more inhibition after
Scopolamine®	2.10 ⁻⁶ Mole/9cm ²	30 h	92 h	120 h
Atropine	"	19 h	42 h	48 h
Antrenyl (Ciba)	"	12 h	74 h	78 h
Probanthine (Searle)	"	2 h	13 h	17 h
Banthine (Searle)	"	0	5 h	5 h 30
Buscopan (Boeringer)	"	0	1 h	2 h
Prantal (Schering)	"	1/4 h	1/2 h	1 h
Homatropine	"	0	1/4 h	1 h

The experimentation of the antisecretory activity showed that the studied substances could be classified as follows: (decreasing activity): Atropine, Scopolamine; Antrenyl, Probanthine, Banthine; Prantal, Buscopan, Homatropine.

Treatment of Hyperhidrosis by Anticholinergics

The reports concerning the treatment of hyperhidrosis by anticholinergics taken by mouth are extremely different and the secondary effects might oblige one to stop the treatment.⁵

The local application by iontophoresis has a limited field of activity. It has been used to treat certain skin lesions which were unfavourably influenced by perspiration, but this is an occasional treatment and purely on medical prescription.

The topical application of these anticholinergic drugs has not given rise to many researches. *Shelley and Horvath* (4) demonstrated that an 18% scopolamine solution applied locally on the skin inhibited the perspiration due to heat. However they very justly called attention to the fact that this treatment is very dangerous as 1 cc of this solution would suffice to kill a man swiftly. *Vultee* (6) treated patients showing excessive sweating of their amputation stumps (consecutive to the application of a prosthetic socket). By local application of Prantal cream (2%) three times daily, he obtained good clinical results.

We carried out some experiments with a cream of Antrenyl. In fact Antrenyl proved to be, in our experiments one of the most efficient among the synthetic or partial synthetic drugs studied by us. Among this group, Antrenyl is also the one prescribed in the smallest doses

by the manufacturer (5 mg tablets).

Our preparation contained 5% active substance in an O/W cream (vanishing cream). It was applied in proportion of 1/2 gr on the arm (2 minutes rubbing, circle of 6 cm of Ø). The place was washed six hours after the application, and the perspiration then induced by a pilocarpine iontophoresis.

No inhibition was ever noted, the place of control showed the same intensity of perspiration as the treated place. It is possible, that the change of the anionic part of Antrenyl molecule facilitate the percutaneous resorption and give better results, but till now one has not examined this possibility.

Conclusion

According to the actual state of knowledge, the treatment of hyperhidrosis per os by anticholinergic drugs does not seem up to the mark, and must be kept to certain special cases. *Sulzberger and Hermann* (5) recently wrote:

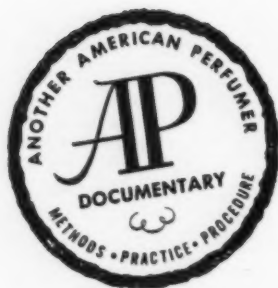
"Reports which we have obtained by personal communications from other dermatologists on the effect of Banthine bromide or Prantal, vary from definitely encouraging to most disappointing. . . . Only extensive further trials can decide whether or not the new compounds are superior to atropine and other, older anticholinergic compounds."

If we considered the topical application of such drugs and suppose that the active compound can penetrate in the skin and truly operate during a certain time, we must also think that its resorption may be strongly increased by lesions of the skin and that its absorption may also be fortuitous; therefore we must beware of the product's toxicity. In the cosmetic field, where numerous users apply the produce daily during long periods it must not be forgotten that an eczematous contact sensitivity might eventually appear.

As everybody knows, certain aluminum salts have been used by millions of people as topical antiperspirants. They seldom create any bother, their activity is proved by numerous tests and their toxicity is quasi absent. Actually no anticholinergic drug seems to combine so many advantages; but it is not out of the question that a substance of that type, appropriate to the topical usage may one day be ready.

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Topical Steroids In Ageing and Senile Skin Cosmetics . . .

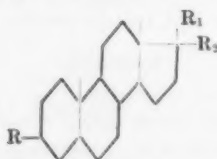
A Patent Digest

*Compounds are now being synthesized
which give beneficial results without at-
tendant estrogenic properties.*

Estrogens have been used in cosmetics for about 25 years. Excessive dosage is guarded against in the directions for use. During this time there has been but one reported case of untoward effect following over dosage of the estrogen-containing cosmetic. This is, indeed, a remarkable record for not even aspirin can claim it.

Even so, manufacturers have been conscious of the possibility of synthesizing related compounds that would have a beneficial effect on ageing skin without the attendant estrogenic properties. To this end, Walter J. Tindall has covered by U. S. and British letters patent the use of substances derived from Δ^5 -androst-3- β -ol or as more descriptively stated in Claim 1 of U. S. Patent 2,845,381 (British Patent 767,824):

"1. Cosmetic preparation for the treatment of human skin, comprising a topical ointment vehicle and at least a single steroid of the formula:



wherein R is a member selected from the group consist-

ing of hydroxyl and oxo, R₁ is of the group consisting of α -ethynyl and α -hydroxyl, and R₂ is of the group of β -hydroxyl and hydrogen."

To explain further the advantages resulting from this invention, the following is quoted directly from the U. S. Patent.

"It has now been discovered that certain substances closely related to the sexually active hormones but themselves substantially free from sexual activity as ordinarily understood, i. e. such as show substantially no activity in stimulating the secondary sex organs, are very effective for the purpose outlined above, and that, in consequence of the absence of sexual activity, the disadvantages previously encountered in such preparations are avoided.

"In accordance with my present invention, a preparation for the treatment of human skin consists of a suitable vehicle capable of being spread on the skin and containing as active ingredient a steroid compound which is virtually free from male or female sexual activity, as herein defined, and is a derivative of Δ^5 -androst-3 β -ol or Δ^5 -androst-3-one or androst-3 β -ol

or androstan-3-one, substituted C17 with a keto group or a hydroxyl group (in either alpha or beta position), with or without an unsubstituted alkyl group which may or may not be saturated, such compounds having 19, 20 or 21 carbon atoms (not counting the carbon atoms of any ester group present); and excluding testosterone and its esters and methyl testosterone.

"As a first example of the substance according to the invention, I mention inactive (non-androgenic and non-oestrogenic) stereoisomer of testosterone (Δ^4 -androsten-17 α -ol-3-one) known as cis-testosterone, which has proved quite satisfactory in experimental stimulation of cell mitosis in the skin.

"A second example according to the invention is Δ^4 -androsteriol-3 β :17 α .

"A third example consists of 17 α -ethinyl- Δ^4 -androsten-17 β -ol-3-one (ethinyl testosterone, commonly called ethisterone), which is virtually inactive both as an androgen and as an oestrogen and has nevertheless proved to be fully active as a skin mitosis stimulant, better in this respect than oestrone.

"In a clinical test, ethisterone in a cream base was applied twice daily to the skin of the arm of aged persons. After twenty-one days, a great change was apparent in the skin structure. There was a great increase in the epidermal thickness almost entirely confined to the layers of living uncornified cells, the outer cornified layers being relatively unaffected. The line of demarcation between the dermis and the epidermis, which is well defined in untreated senile skin, became again partially obscured, as it is in normal youthful skin, by the marginal spines of the basal cells of the stratum germinativum. The basal cells became enlarged. The dermal papillae producing the folded appearance of the dermal-epidermal junction was virtually absent in the untreated state, but after treatment the development of these papillae had returned virtually to the normal youthful state.

"The above listed substances are also virtually inactive as an androgen or as an oestrogen and have proved to be fully active as skin-mitosis stimulants.

"The following list of substances shows further examples of substances which can be used according to the invention

- (4) Δ^4 -androsteriol-3 β :17 β
- (5) 17 α -methyl- Δ^4 -androsteriol-3 β :17 β
- (6) 17 α -ethyl- Δ^4 -androsteriol-3 β :17 β
- (7) 17 α -vinyl- Δ^4 -androsteriol-3 β :17 β
- (8) 17 α -ethinyl- Δ^4 -androsteriol-3 β :17 β
- (9) 17 α -ethyl- Δ^4 -androsten-17 β -ol-3-one (17 α ethyl testosterone)
- (10) 17 α -vinyl- Δ^4 -androsten-17 β -ol-3-one (17 α vinyl testosterone)
- (11) Androstanediol-3 β :17 β
- (12) Androstanediol-3 β :17 α
- (13) 17 α -methylandrostanediol-3 β :17 β
- (14) 17 α -ethinylandrostanediol-3 β :17 β
- (15) 17 α -vinylandrostanediol-3 β :17 β
- (16) 17 α -ethylandrostanediol-3 β :17 β
- (17) Androstan-17 β -ol-3-one
- (18) Androstan-17 α -ol-3-one
- (19) 17 α -methyl-androstan-17 β -ol-3-one
- (20) 17 α -ethyl-androstan-17 β -ol-3-one
- (21) 17 α -vinyl-androstan-17 β -ol-3-one
- (22) 17 α -ethinyl-androstan-17 β -ol-3-one
- (23) Androstanedione-3:17
- (24) Androstan-3 β -ol-17-one (epiandrosterone)
- (25) Δ^4 -androsten-3 β -ol-17-one (dehydro-epiandrosterone)
- (26) Δ^4 -androstenedione

"As applied to a cosmetic cream, the present invention

is also concerned with the nature of the cream base utilized for the incorporation of the sexually inactive steroid compounds herein referred to. As heretofore compounded, such creams commonly included a proportion of cholesterol either as a special incorporated component of the cream or as a constituent of lanolin which is frequently employed as a cream base constituent. However, it is already known that cholesterol promotes the absorption of lipid-soluble substances through the skin and that the removal of cholesterol from the skin and from the base vehicle retards or inhibits such absorption.

"According to a further feature of the invention, a cream base or vehicle for the application to the skin of the steroid substances of the invention, is, therefore, made up without any cholesterol, thus ensuring that the active substances are retained in the skin and not passed to any appreciable extent into the general circulation. In this way, the action of the active substances is confined for the major part of the surface layers of the skin with a consequent improvement in the efficiency of the application of the cream.

"Such a cream base may consist mainly of water, glyceryl monostearate and glycerine with a small proportion of arachis oil and of cetyl alcohol.

"The amount of active substance which may be incorporated in a cream base either of the above character or of the more conventional lanolin based types may vary within quite wide limits. The upper limit is however generally set by the relatively low solubility of the active substance in an organic solvent capable of being added to and mixed with the cream base. A convenient solvent for this purpose is propylene glycol. The lower limit is set by a figure below which there is insufficient of the active substance present to produce any useful effect. Under normal circumstances and to obtain a cream having a practically useful effect it may be said that the amount of active substance varies from the maximum amount that can be incorporated in the final ointment, taking into account the solubility of the substance in an organic solvent, and the lower limit may be perhaps one-tenth to one-twentieth of that amount depending partly on the purpose of use of the ointment and the particular selected substance used. The following Examples 1 to 7 illustrate ointment-like preparations according to the invention based on the use of a non-cholesterol cream base:

Example 1

"A cream base consists of the following substances, the proportions being by weight:

	Parts
Glyceryl monostearate	15
Arachis oil	5
Cetyl alcohol	1
Glycerine	10
Water	100

"The glyceryl monostearate and the glycerine are mixed with the water with a small amount of the arachis oil and cetyl alcohol, and then the rest of the last named substance added with continued mixing. In the preparation of a cosmetic cream, a quantity of ethisterone (17 α -ethinyl- Δ^4 -androsten-17 β -ol-3-one) is dissolved in sufficient organic solvent such as propylene glycol to dissolve it and the latter solution is then added to and intimately mixed with a cream base compounded as above explained. The amount of ethisterone added as an active substance is such that 1 to 10 mg. thereof is present in every ounce

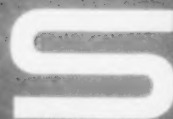


LIGNYL ACETATE

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NEW YORK

of the finished cream.

Example 7

"To a cream base of the character disclosed in Example 1 there is added with thorough mixing a solution of 17 α -methylandrostan-17 β -ol-3-one in an organic solvent. The amount of the above substance present is such that 2 to 15 mg. are present for each ounce of the cream base.

"Other types of base or vehicle can be used for other purposes. For example, an ethical medical preparation may be used as the vehicle in the case of a preparation for the treatment of burns, while an oil is suitable for certain other medicinal treatment preparations.

"The invention is not of course specifically restricted to the use of non-cholesterol bases; the use of such bases is desirable as inhibiting the absorption of the active substances through the skin. The following is an example showing the use of a cholesterol-containing base:

Example 8

"A lanolin base is made up by mixing the following ingredients, the parts being given by weight:

	Parts
Cetyl alcohol	1
Sodium alginate	1
Glycerine	1
Wood alcohol BP	30
Arachis oil	5
Water	62

"The above compounds are thoroughly mixed together to form a soft cream to which is added a solution of Δ^4 -androsten-17 β -ol-3-one dissolved in organic solvent to such an extent and the amount of such solvent being such that the resulting base contains 2 to 5 mg. of the active substance per ounce of the finished cream."

British Patent 768,129

Cosmetic Preparations for the Treatment and Care of the Skin
Ciba, Limited, Basle, Switzerland

"This invention provides cosmetic preparations for the treatment and care of the skin, which contains as a base substances of oily, fatty or waxy consistency known to be suitable for use in such preparations, and which also contain pregnenolone (Δ^5 -pregnene-3 β -ol-20-one) and/or an ester thereof, for example, pregnenolone acetate and/or an ether thereof, for example, pregnenolone benzyl ether.

"The word 'known' is used herein to mean known in the literature of the subject. The invention is based on the observation that pregnenolone and/or an ester and/or an ether thereof stimulates the growth of the epidermis, and lead to an increase in the layers of epidermis cells and to cell proliferation accompanied by enlargement of the nuclei and cytoplasm, and that therefore these compounds are of advantage as agents for the care of the skin. Thus, for example, they impart to ageing skin a youthful and firm appearance and remove wrinkles.

"In preparing the new skin preparations the substances of oily, fatty or waxy consistency known to be suitable for use in such preparations are mixed with pregnenolone and/or an ester and/or an ether thereof. The preparations can be made up as cream-like or liquid emulsions. As substances known to be suitable for use as a base in cosmetic preparations for the treatment and care of the skin there may be mentioned aliphatic hydrocarbons, such as yellow petroleum jelly, triglycerides

such as, for example, as hog fat, cocoa butter, almond oil, saturated or unsaturated higher fatty acids such as myristic acid, undecylenic acid, oleic acid or esters thereof, Peru balsam or chlorophyll. It is of special advantage to add an ester or ether of benzyl alcohol, for example, the benzyl ester of lauric acid, oleic acid or cinnamic acid, or dibenzyl ether, and especially the benzyl ester of benzoic acid or of naphthoic acid. These additions increase the action of the pregnenolone and/or an ester and/or an ether thereof, that is to say, in order to obtain the same effect a substantially smaller quantity of pregnenolone and/or an ester and/or an ether thereof can be used. Furthermore, it is of advantage to add substances which stimulate the blood circulation in the skin, such as nicotinic acid amide.

"The following examples illustrate the invention, the parts being by weight:

Example 3

"The following ingredients are melted together on a water bath:

0.2 part of pure pregnenolone;
10.0 parts of bleached beeswax;
10.0 parts of hydrogenated ground nut oil;
5.0 parts of benzyl laurate;
5.0 parts of spermaceti;
35.0 parts of almond oil, preserved;
2.5 parts of lanoline;
1.7 parts of sorbitan sesquioleate and
0.8 parts of cholesterolin

and the melt is heated until it has become clear and reached a temperature of 80°C. There are also mixed together

3.0 parts of glycerine;
0.2 part of magnesium sulphate;
0.6 part of borax, and
26.0 parts of distilled water

and the mixture is heated to 80°C. The strained melt at 80°C. is emulsified in the usual manner with the filtered aqueous solution having a temperature of 80°C., and the mixture is stirred until cold. At 40°C. there is added a mixture of perfume oils. The mixture is then further stirred until it has cooled to 25°C. There is obtained a fattening skin cream.

Example 4

"The following substances are melted together on a water bath:

0.2 part of pure pregnenolone;
6.0 parts of stearic acid;
2.0 parts of α -naphthoic acid benzyl ester;
0.3 part of cetyl alcohol;
0.3 part of sorbitan mono-oleate;
1.5 parts of polyalkylene oxide-sorbitan mono-stearate and
0.2 part of para-hydroxybenzoic acid methyl ester, and the

melt is heated until it has become clear and reached a temperature of 80°C. There are also mixed together

2.3 parts of triethanolamine oleate;
3.0 parts of glycerine and
84.2 parts of distilled water

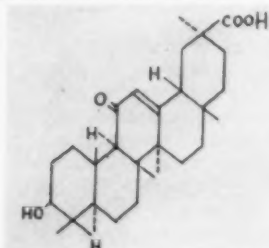
and the mixture is heated to 90°C. After filtration at 88°C. it is emulsified in the usual manner with the strained melt at 80°C., and the mixture is brought to 40°C. with intensive mixing. A quantity of a mixture of perfume oils is added and the whole is thoroughly mixed while cooling to 25°C. There is obtained a face milk of medium viscosity."



GLCYRRHETINIC ACID

An Introduction

Glycyrrhetic Acid, a triterpene is a sapogenin derived from liquorice root (*glycyrrhiza glabra*) and is the aglycone of the sweet principle of liquorice. It has the following structural formula:—



This compound was first mentioned by Gorup-Besanez¹ in 1861 and since that date many research workers have attempted to elucidate its structural formula. This has only recently been achieved. Glycyrrhetic acid is a white crystalline flocculent powder of 3 micron or less particle size. It is tasteless and odourless.

From the size and structure of the molecule it was only natural to expect stereo isomers. Two isomers (α and β) have been described in 1955 by Beaton and Spring² and a third isomer (γ) has been mentioned by Benigni and Franco³ in 1958.

Early clinical trials reported mainly in the British Medical Journal were contradictory, but when the pure active isomers (tested biologically) were used, the reports were very favourable.⁴⁻⁷

It has been shown pharmacologically⁸⁻⁹ that different isomers of glycyrrhetic acid have varying degrees of anti-inflammatory activity. The activity seems to be

influenced by the location of the crop, the time of gathering, the age of the roots and, of course, the method of hydrolysis. Successful results have been obtained by a form of enzymatic hydrolysis.

Synthetic derivatives have been prepared which are water soluble and more active. Most of the chemical research has been carried out in England by a research team of Biorex Laboratories Ltd., London, headed by Professor E. E. Turner, F. R. S., Bedford College, University of London, and a number of Patents have been applied for.

Glycyrrhetic acid has been found of great value in the treatment of subacute and chronic inflammatory dermatoses, diseases of the eye and other inflammatory conditions where topical application is possible. It is available in the form of a 2% Ointment. It has also been found of great value in burns and in varicose ulcers where tissue breakdown occurred. The newer derivatives, being soluble, have been found of value in the treatment of a number of conditions such as inflammation of the gastro-intestinal tract including ulcerative colitis, inflammation of the joint, allergic conditions such as asthma, hay fever, bronchospasm, urticaria and various endocrine conditions.

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THE RATIONAL USE of GLCYRRHETINIC ACID in DERMATOLOGY*

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For many generations the concentrated aqueous extract of the root of *glycyrrhiza glabra* has been of pharmaceutical interest as a demulcent and as a flavouring and sweetening agent. Recently, however, the sweet tasting glycoside from liquorice has attracted much attention because of its biological activity. In this article I shall discuss the results obtained from the topical application of the anti-inflammatory triterpene, glycyrrhetic acid (G.A.), obtained from liquorice, in a series of 124 cases and I shall later review briefly its chemistry and pharmacology.

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In my trial I have found that ointments containing the active isomers of G.A. when applied topically, have a marked anti-inflammatory action in a variety of dermatoses, mainly of the subacute and chronic type, without causing the 'rebound' phenomenon when they are discontinued. Combined with old and well tried dermatological remedies such as coal tar and salicylic acid, these isomers of G.A. were shown to possess a synergistic action and to give relief in many recalcitrant conditions. Synergism has also been found to exist with Neomycin.

An extensive and varied correspondence has appeared

in the columns of the *British Medical Journal*, some authors having damned G.A. and others having praised it. It became apparent that clinicians who had carried out a trial on a sufficiently large number of cases with what is called 'the active isomers' of G.A. claimed good results (Evans, 1956; Chakravorti, 1957; Annan, 1957; Colin-Jones and others, 1957). However, another group of clinicians who reported mostly on small-scale trials found the G.A. they employed useless (Bettley, 1956; Warin and others, 1956; Donaldson and others, 1956; McCallum, 1956). I therefore decided to institute a thoroughly controlled trial where reasonable numbers of cases of various patterns of eczema might create a statistically significant picture.

The trial was carried out both on in-patients and out-patients, at the General Hospital, Margate, Haine Hospital, Ramsgate, and the Queen Victoria Memorial Hospital, Herne Bay, as well as in my own practice.

Sommerville (1957) has stated "There has been an almost unseemly rush to be in at the death of a new drug." For some time clinicians have realized that hydrocortisone in dermatology is an 'open Sesame' word (Annan, 1957) due probably to the fact that hydrocortisone was heralded as a wonder drug in the international lay press. For this reason hydrocortisone has in many cases, a strong psychosomatic curative action. Yet in actual fact the value and field of action of hydrocortisone has been shown to be quite limited. The relief given, though so often dramatic, is frequently only temporary and the well-known 'rebound' phenomenon often occurs. The fact that hydrocortisone can influence the reaction to pruritus and allergic skin manifestations when applied topically in the form of an ointment, does not necessarily depend on the fact that it is a steroid or corticoid hormone. On the other hand, from earliest times medical literature has attributed to the weed liquorice such powers as the depressing of inflammatory reactions of the throat and chest, and later of the stomach and duodenum. G.A., the aglycone of the sweet principle of liquorice, in its pure form, has been found to possess anti-inflammatory, anti-pruriginous and healing properties when applied topically.

All the usual hazards of assessing the value of a new drug in skin diseases were realized. As far as possible in this trial patients on G.A. were given no more reassurance or 'psychotherapeutic' encouragement than any other patient. Even symmetrical comparison cases were merely told to report which ointment suited them best. Independent observation of the results was possible in most cases and I tried to be as severe and objective as possible.

A comparison of an ointment containing the active isomers of G.A. (Biosone G.A.) and the base has been published (Colin-Jones, 1957) and I have thought it unnecessary to repeat a comparison as I used the same ointments.

Comparison of G.A. and Hydrocortisone

Table I gives my results in a trial on 43 cases. All these cases were controlled either by symmetrical comparison or against previous hydrocortisone treatment. Where a greasy or non-greasy G.A. preparation was used the corresponding greasy or non-greasy hydrocortisone preparation was also used.

While I was carrying out the comparison with hydrocortisone a pattern very soon emerged which indicated to me that the effect of the two substances was not identical and that it often differed considerably.

Table I
Comparison of G.A. and Hydrocortisone

Conditions	Drug	No. of Cases	Marked Improvement	Some Improvement	No effect or worse
Contact and Allergic dermatitis	Hydrocortisone	14	11	2	1
	Glycyrrhetic Acid	14	10	3	1
Eczema of the hands	Hydrocortisone	7	3	2	2
	Glycyrrhetic Acid	7	4	2	1
Infantile eczema	Hydrocortisone	5	5	-	-
	Glycyrrhetic Acid	5	2	2	1
Anogenital pruritus	Hydrocortisone	4	1	2	1
	Glycyrrhetic Acid	4	4	-	-
Hypostatic and Varicose eczema	Hydrocortisone	3	2	-	1
	Glycyrrhetic Acid	3	2	1	-
Neurodermatitis	Hydrocortisone	3	1	1	1
	Glycyrrhetic Acid	3	3	-	-
Eczema of various patterns	Hydrocortisone	7	5	1	1
	Glycyrrhetic Acid	7	6	1	-
TOTAL	Hydrocortisone	43	28	8	7
	Glycyrrhetic Acid	43	31	9	3

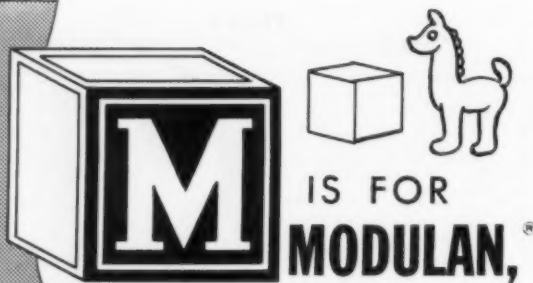
Hydrocortisone was better as a rule in acute eczemas and infantile eczema, whilst G.A. was usually better in chronic or subacute conditions, for example, long-standing anogenital pruritus and neurodermatitis, especially when inflammatory and pruritic. In view of this finding, only G.A. was used in the later cases, with or without other substances.

It has been stated (Scott, 1957) that in a controlled trial (Tillman, Crow and Scott, 1956, unpublished data) an ointment containing G.A. was soothing but that no significant difference between the ointment itself and the control was revealed. In my comparison of G.A. and hydrocortisone, I have found that in 26 cases the response to the two drugs was almost identical and in the 17 cases where the response was different, 16 were improved with glycyrrhetic acid and 12 with hydrocortisone. In the absence of the published data, it is impossible to tell whether the active isomers of G.A. were used in the other trial.

Table II shows the 124 cases treated with ointments containing the biologically active isomers of G.A. as supplied to me under the trade name of Biosone G.A.

It is an extremely good result for 73 per cent of the cases treated to have either cleared or shown marked improvement and for a further 20 per cent to have improved to a lesser degree.

From this table it can be seen that in the group of 28 cases of contact and allergic dermatitis, improvement in varying degrees was found in 27 cases, only 1 case did not respond. In eczema of the extremities and anogenital pruritus the results were superior to those I would have expected from other forms of treatment. In infantile eczema 7 out of 9 cases showed improvement, but in view of the small number of cases treated I feel that these results are somewhat inconclusive. In hypostatic and varicose eczema, where more often than not there is a great deal of ulceration or excoriation, all 10 patients showed improvement—a very gratifying picture in such an ungrateful condition. In neurodermatitis the drug has proved remarkable, as out of 8 cases all of them showed marked improvement. In seborrhoeic eczema 7 out of 8 responded, and in 8 cases of infected and pustular eczema all responded. The same satisfactory picture was obtained in a variety of



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other patterns of eczema, where out of 17 cases all showed response.

From these cases it becomes evident that G.A in its biologically active form is a valuable drug in the treatment of various eczematous manifestations, and the response in the 124 cases has proved its efficacy.

I summarize below a relevant case history.

Case No. 1. Miss E. N. aged 65, a housekeeper, was first admitted to hospital in April, 1953, suffering from acute dermatitis venenata affecting particularly the whole face, neck and arms. Her skin and scalp were of seborrhoeic type. Normal saline compresses followed by soothing preparations of calamine were used and sulphacetamide eye ointment (6 per cent) for the eyes.

Table II
Patients Treated With Biosone G.A.

	Total	Cleared or Marked Improvement	Improvement	No effect or worse
Contact and allergic dermatitis	28	21	6	1
eczema of the extremities	12	9	2	1
Anogenital pruritus	11	8	2	1
Infantile eczema	9	5	2	2
Hypostatic and varicose eczema	10	5	5	—
Neurodermatitis	8	8	—	—
Psoriasis	13	8	3	2
Seborrhoeic eczema	8	6	1	1
Infected and pustular eczema	8	7	1	—
Various patterns of eczema	17	14	3	—
TOTAL	124	91	25	8
	%	73%	30%	7%

She was discharged 5 weeks later, but her skin was still unsettled from persistent scratching. I re-admitted her to hospital with a recurrence of the same condition in April, 1954. Similar orthodox treatment was administered with similar results and she was discharged in June, 1954, after 7 weeks.

She was re-admitted to hospital on 8th April, 1957, with another severe recurrence, and Biosone G.A. Ointment with Neomycin was used on the face and neck only, and orthodox treatment on the hands. The patient was photographed on admission (Fig. 1). On 13th



Fig. 1. Miss E. N. Skin condition before treatment.



Fig. 2. After 5 days' treatment. The skin has cleared.

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April the face and neck were vastly better and she was photographed again on 15th April, 1957 (Fig. 2), but the hands on orthodox treatment were more stubborn. The face cleared dramatically. The patient was discharged on 1st May, 1957.

A month later the patient returned with a severe chronic eczema of the hands and wrists which were then treated with Tar-Biosone G.A. non-greasy, with good results. At this stage there was no recurrence of the symptoms of the face and neck. All three major attacks occurred in April and spring cleaning may have been one of the causes.

She was in hospital for two periods of 5-7 weeks on orthodox treatment, but on the third occasion the areas treated with G.A. with Neomycin cleared completely in 1 week, but her hands took much longer using the previous treatments, and cleared well and quickly when put on G.A. with Tar (Tar Biosone G.A.).

For some time I have used hydrocortisone in conjunction with other well tried remedies such as zinc oxide and tar, and in infected cases an antibiotic. I find that this has also been reported in America (Welsh and Ede, 1954; Bleiberg, 1956; Clyman, 1957) showing good results and eliminating the 'rebound' effect so common when hydrocortisone is used alone. In the later stages of my trial I have investigated the claim of synergism between G.A., tar and salicylic acid. Table III shows my results.

Conditions	No. of Cases	Marked Improvement	Some Improvement	No Effect
Psoriasis	12	7	3	2
Neurodermatitis	3	3	—	—
Chronic eczema of the extremities	5	5	—	—
Various chronic eczemas	3	2	1	—
TOTAL	23	17	4	2

The cases in Table III were controlled, either directly or with previous treatment, against tar and salicylic acid and the excellent results obtained are, I feel, attributable to the synergistic combination of the active G.A. with tar and salicylic acid, as illustrated below:

Case No. 2. Mr. E. M., aged 67, had had a 7 years' history of eczema of the legs, hand and arms, with intolerable itching and burning. First treated by me in January, 1956, with the usual conventional remedies including tar, salicylic acid and zinc ointments. Some improvement was noted but the pruritus was not relieved and there was a great deal of lichenification. In October, 1956, he was referred for a second opinion to a London teaching hospital. This confirmed my diagnosis of neurodermatitis and agreed that hydrocortisone was not suitable in his case. Pyrotherapy was recommended.

The patient was admitted to hospital for intravenous T.A.B. with good results. In December, 1956, there was a further breakdown and conservative treatment of tar in zinc paste was continued. In January, 1957, there was some impetiginization of face and scalp. By February, 1957, the impetiginized eczema of face and scalp had cleared on Aureomycin ointment ($\frac{1}{2}$ per cent), but the lower trunk, legs and forearms, left shoulder and axilla still had a chronic licheniform eczema, with general adenitis. The diagnosis of Hodgkin's disease and so on was considered. Biopsy of skin, however, showed only a low grade non-specific, chronic inflammatory reaction in the dermis and a biopsy of a lymph node from the groin showed a histological picture of lipo-melanotic reticulosis (dermatopathic lymphadenitis) with no sign of malignancy. In June, 1957, Tar-

Biosone G.A. Ointment with Salicylic Acid, greasy, was applied. Within a few days there was a marked improvement, with less itching, and the skin became softer and less scaly. By the middle of July, after 4 weeks' treatment, he was vastly better, and the glands were smaller. This improvement is still maintained.

Case No. 3. Mr. G. M., aged 45, had suffered from psoriasis of the elbows for 16 years and of the hands for 9 months, which had been made worse by contact with detergents during his work as a barman. He had been treated before I saw him with Psorax, Pixyl and Pragmatar, without any real benefit. Tar-Biosone G.A. Ointment with Salicylic Acid was started on 3rd July, 1957, and by 17th July, 1957, he was much improved. Improvement continued and when last seen at the end of August the condition was still well under control.

Case No. 4. Mrs. P. G., aged 52, a housewife, was first seen in June, 1956, suffering from severe pustular psoriasis of both feet. Scrapings were negative for fungus. She was treated with reassurance, crude coal tar in Lassar's paste, and many other similar preparations. In July, 1957, the condition flared up and she became grossly depressed and, as she said, "desperate." Tar-Biosone G.A. Ointment with Salicylic Acid, greasy, was used, and in 14 days there was a satisfactory improvement, but not dramatic, and small doses of superficial x-ray were prescribed in addition. She improved dramatically in the following 2 weeks, well before the superficial x-ray could have been really effective, and she was much more relaxed. She is now almost clear.

Evidently G.A. in such intractable conditions as psoriasis can prove dramatic in its action, and has in many cases made life more tolerable for the patient. It is in these intractable skin conditions, and some where the aetiology is obscure, that G.A. has its greatest value as it offers to the clinician a new approach to hitherto recalcitrant dermatoses.

During this trial neither contra-indication nor sensitivity to this drug has become evident. A very occasional but transient feeling of burning has been met, but this seems to disappear when the application is continued.

I have used G.A. with Neomycin in painful ulcerative conditions of the mucous membranes with great relief, but in not enough cases to be statistically significant.

Chemistry

G.A. is the aglycone of glycyrrhizic acid, the sweet constituent of liquorice extract. This acid is a pentacyclic triterpene containing one hydroxyl group, one carboxyl group and a conjugated cyclic keto grouping which is characterized by an optical absorption in the ultra violet near 250 μ . Beaton and Spring (1955) described α and β isomerism about the 18 carbon atom and in such a large molecule it is more than probable that further isomers and/or other acids exist in the commercial mixture commonly termed "glycyrrhetic acid".

Pharmacology

It may be significant that a characteristic group of corticosteroids, that is the conjugated cyclic keto grouping, is also present in G.A. This may explain why this compound has attracted attention in connection with the treatment of Addison's disease, rheumatoid arthritis and duodenal ulcers. Liquorice compounds have been investigated by Revers (1948) who established that succus liquoritiae had a therapeutic effect on ulcer ventriculi. Verheyen (1948) suggested that this favourable influence on ulcers was due to the spasmolytic action of liquorice juice. Hart (1957) suggested that



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G.A. was a mild mineralocorticoid. Somers (1957) found that G.A. acts in a similar way to cortisone in depressing the reaction to tuberculin in B.C.G. sensitized guinea pigs. D'Arcy and Kellett (1957) also found that G.A. depressed the formation of granuloma tissue induced by subcutaneously implanted cotton wool pellets in a test on rats as described by Meier and others (1950). Logemann, Lauria and Tosolini (1957) independently published similar results. At the Summer Meeting of the British Pharmacological Society (Oxford), 1957, D'Arcy, Kellett and Somers demonstrated that certain biologically active fractions of G.A. (Biosone G.A.) have a marked anti-inflammatory action, whereas a sample of "commercial glycyrrhetic acid," from an entirely different source, showed no anti-inflammatory activity at all.

Kasuko Ito and Kazuro Kuroda (1955) have demonstrated the action of crude liquorice extracts administered orally in some dermatoses and in 4 cases out of 11 alopecia areata they state that evidence of regrowth of hair on the scalp was observed.

Pozzo (1957) has shown that glycyrrhetic acid ointment, either alone or in combination with antibiotics, has a marked antiphlogistic value when applied topically in eczematous skin conditions, without after-effects.

Summary

A clinical trial has been described on various patterns of skin manifestations covering 124 cases. The evidence strongly suggests that biologically active isomers of glycyrrhetic acid have a marked anti-inflammatory action and have been found effective in a variety of dermatoses. As a result of this trial, I have come to the conclusion that G.A. is more effective than hydrocortisone in the subacute, chronic and intractable skin conditions. Its effect on ulcerated mucous membrane is mentioned. It has not sensitized the patient when applied topically, no contra-indications have been found and it has brought relief in cases where other forms of therapy have failed. Its pharmacology has been reviewed and it has been shown that, in spite of its structural resemblance to hydrocortisone, it differs by being a non-steroidal substance with an action differing from that of hydrocortisone.

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Neomycin appears to be an eminently practical antibiotic for topical use in the elimination of normal axillary odor.

H. A. NELSON*

The original observations on the relationship between bacteria and axillary odor were made by Killian and Panzarella¹ in 1947 and by Shelly *et al*² in 1953, and numerous studies have since been carried out on odor prevention with chemical bacteriostats both in soaps and topical preparations. The history of the development of the antibacterial approach to deodorizing the axillary area has been reviewed by Klarmann³ in a paper discussing the chemical and bacteriological aspects of antiperspirants and deodorants. It has more recently been reported by Blank *et al*⁴ that aluminum salts commonly used as antiperspirant drugs exert an antibacterial action against many common skin bacteria.

There is considerable range of individual preference as to the use of an antiperspirant or a deodorant, or a combination of the two. It is quite apparent, however, that unless there is a deodorizing effect, and it is now realized that this means an antibacterial effect, a product will be unacceptable since it is recognized that antiperspirants restrict and do not stop the flow of perspiration. Therefore most products contain deodorant drugs whether or not they contain perspiration inhibitors.

Chemicals with the ability to kill or inhibit bacterial growth may reduce axillary odor formation, but there are several additional requirements for such a drug in an acceptable cosmetic product. It should be stable for long periods, compatible with a wide range of substances, colorless, odorless, nonirritating, and nontoxic. Most of the available antibacterial agents fail in one or more of these areas. The antibiotic neomycin seems to meet the requirements more completely than does any other compound.

Shelley and Cahn, writing on antibiotics in Control of Axillary Odor in the recent book *Neomycin*, Waksman⁵, have commented that neomycin appears to be an eminently practical antibiotic for topical use in the

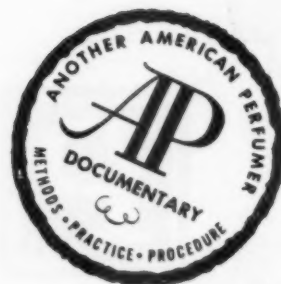
elimination of normal axillary odor. The first observations on the utility of neomycin as a deodorant were made in 1955 by Shelley and Cahn⁶ who reported complete inhibition of axillary odor in men using neomycin sulfate cream or lotion.

Subsequently a new antibacterial antiperspirant based on the activity of neomycin was developed and clinically evaluated on an extensive scale. Some of these studies have been reported by Robinson and Robinson⁷ and Hoekenga⁸. In their summary, Robinson and Robinson state their opinion that, "Deocin, an antibacterial-antiperspirant, is superior to most of the presently available deodorant preparations." Hoekenga reported complete odor control in a series of tests during a period of high heat and humidity in Panama.

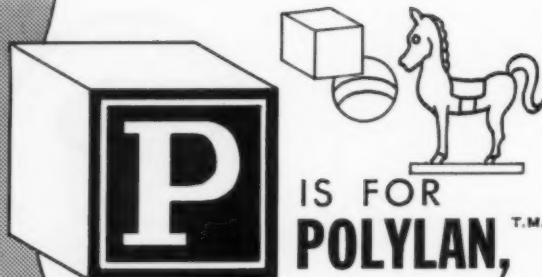
Differs From Other Antibiotics

Although neomycin is an antibiotic, it differs in several important respects from other antibiotics and overcomes many of the objections that may be raised to antibiotics as routine topical agents. Of outstanding importance is the fact that neomycin is bactericidal rather than bacteriostatic. Largely due to this fact, the development of resistant strains of bacteria is not a serious problem. In the entire history of topical neomycin there is no report of the development of a resistant bacterial strain during therapy. The index of sensitization to neomycin is also very low, and is not complicated by parenteral use of the drug, as it is used primarily topically and orally. Neomycin is not significantly absorbed when used topically or orally.

The background for the clinical acceptability of neomycin in deodorant products is found in the extensive and favorable medical history of topical neomycin as exemplified by the reports of Livingood *et al*,⁹ Church,¹⁰ Forbes and King,¹¹ and many others. These papers report very favorable clinical experience in the treatment



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of various skin infections with topical neomycin, and demonstrate the high rate of effectiveness of neomycin against skin pathogens, especially staphylococci, which have also been shown to be important in odor formation.

Formulation

In the clinical history of topical neomycin, which has extended over the past nine years, ointment, cream and lotion formulations have been used with generally comparable results in a great variety of skin infections. These formulations have usually contained about 0.35% of neomycin activity (from the sulfate salt). The incidence of sensitization reports has been very low, and neomycin topical products are currently the therapy of choice for most skin diseases.

For deodorant preparations, creams or lotions containing 0.5% neomycin sulfate can be prepared and are relatively stable. The following combinations have been reported in the literature (Forbes) and are representative types of satisfactory formulation.

Water Miscible base

Neomycin Sulfate	5 mg/gm
Carbowax 4000	
Carbowax 1500	
Tween 20	
Propylene Glycol	

Cream

Neomycin Sulfate	5 mg/gm
Tegacid Regular	
Polysorbate 80 USP	
Propylene glycol USP	
Spermaceti USP	
Methylparaben USP	
Distilled water q.s.	

Lotion

Neomycin Sulfate	5 mg/cc
Methylparaben USP	
Butyl Parahydroxybenzoate	
Tegacid Regular	
Propylene glycol USP	
Polysorbate 80 USP	
Spermaceti	
Distilled water q.s.	

The stability and compatibility of neomycin permit its inclusion in various formulations. Dale and Rundman¹¹ have discussed the compatibility of neomycin with many ingredients common to cosmetics and pharmaceuticals, and have described stability studies with various combinations. It is especially noteworthy, from a formulation standpoint, that neomycin sulfate, which is highly water soluble, is stable in aqueous solution over a pH range of from 2 to 10, and can be held at 120°C for 15 minutes without significant loss of activity.

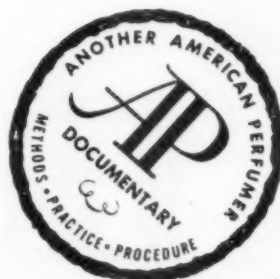
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THE TREATMENT of ACNE with COSMETIC PREPARATIONS

IRWIN I. LUBOWE, M. D., F. A. C. A.*



The specific etiology of acne vulgaris has not definitely been established. Significant studies have been made in the last few years in evaluating the contributing and related factors. The causal factors in the production of acne are believed to be the following:

- 1) Endocrine dysfunction;
- 2) Dietary indiscretion;
- 3) Gastrointestinal disturbance; constipation
- 4) Focal infection;
- 5) Allergic diathesis;
- 6) Variations in temperature and humidity, with increased perspiration.

With the onset of adolescence there is brought into activity disturbances of the hormone secretion, activation of the pilosebaceous system, dietary indiscretions and commencement of tensions which surround the social awakening and responsibilities of the teenager.

The relationship between acne vulgaris and the hypersecreting sebaceous glands has been described by Lubowe (1) who demonstrated the estrogen-androgen imbalance. This type of acne is usually observed in the early adolescent patient and frequently is associated with a premenstrual flare-up. In the female, it is associated with the irregularity of menses, scant menses and dysmenorrhoea. In the male, it is identified with an oily greasy skin, associated with seborrhoeic dermatitis of the face, chest, back and scalp.

There is a deviation in the ratio of the daily urinary excretion of androgen to that of estrogen which is usually 8.9 mgm. in the male. In the active acne patient it is sometimes increased to almost 19.8 mgm.

The above constitutional factors must be treated by a physician or dermatologist. However, in this paper, our special interest is with the function of cosmetic preparations which will aid the user in reducing or masking the discomfort of the blemishes, and the direct therapeutic effect of the cosmetic preparation upon the comedones, pustules, cysts and scars.

The importance of diet cannot be over-emphasized. Basically, foods possessing high amounts of carbohydrates or fats must be avoided. We believe that the excessive intake of these unwarranted foods causes a disturbance in the lipid metabolism and stimulate the over-activity of the pilosebaceous glands with outpouring of the greasy sebum. There also seems to be a disturbance in keratinization of the epithelium which constitutes the follicular opening of the sebaceous duct and as a result, there is a closure of the ostium. The sebaceous material is still being excreted. However, without the presence of an unobstructive opening the secreted sebum collects, solidifies and thus is formed a comedone which is initially colorless or white, and eventually darkens because of oxidation. With secondary infection there may develop a pustule, follicu-

litis, granuloma and/or cyst. If the folliculitis and infection extend to the subcutaneous layer below the epidermis, healing with residual scarring takes place. The residual scars can be effectively treated by peeling preparations or dermabrasion.

The acne can be divided into several types:

- 1) The acne comedones—consisting basically of whiteheads;
- 2) Acne papulosa—consisting basically of papules;
- 3) Acne Pustulosa—consisting of infected papules; pustules or follicles;
- 4) Acne conglobata or acne cystica—consisting of enlarged cysts which extend below the subcutaneous area;
- 5) Residual acne scarring—which follows acne which has become secondarily infected.

Cosmetic Treatment

Cosmetic preparations when properly used are very efficacious in reducing the papules, the pustules, and clearing the secondary infection, improving the skin texture, normalizing the functioning of the epidermis, and finally, simultaneously masking the acne lesions, and healing them therapeutically.

The following dermatological preparations have been found to be effective and made elegant as cosmetic formulations. They can be altered to suit the specific need of the involved skin:

1) Lotia Alba (USP):

Zinc Sulfate	4.0
Potassium Sulfurata	4.0
Aqua Distillata qsad	100.0

It has been used by dermatologists for time immemorial. Aqua Rosea or scented witch hazel can be used as a vehicle. It can be made into a mild 4% or a concentrated 8% lotion. The preparation must be utilized in fresh state; or it loses its therapeutic activity. There is a commercial preparation on the market which contains the zinc sulfate and the potassium sulfurata in powder form, encased in a paper envelope, which is prepared freshly by the patient, thus assuring its therapeutic activity.

2) Kummerfeld's lotion:

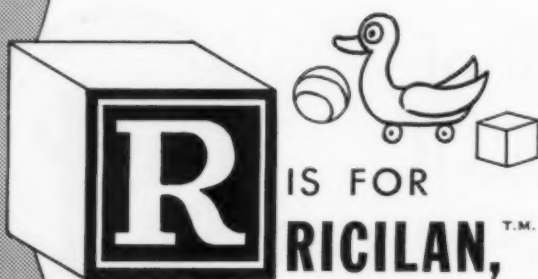
Camphor	1
Acacia (in the powder)	2
Glycerine	4
Precipitated sulfur	10
Rose water to make	100.0

This pleasant formulation dries very quickly and produces a fine covering of sulfur and possesses the peeling and stimulating action of camphor. It is frequently used in the subsiding type of acne when there is minimal amount of lesions, and the stimulation of the epidermis is desired.

3) Foundation acne lotion:

Neutractor	1.0-5.0
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*Clinical Professor in Dermatology, New York Medical College Metropolitan Medical Center Hospital, New York, N.Y.



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Resorcinol	2-6
Ppt. sulfur	2-6
Zinc Oxide	
Calamine	
Glycerine	aa 10.0
Water	
Spiritus	aa 40.0

This popular formula can be used in various shades, containing neutracolor which is a commercial name for combinations of ferric oxide and bentonite. The foundation lotions are either made up in a thick liquid base or a compressed powder, and easily applied. More recently I have been conducting clinical studies with Aluminum Allantoinates and DL Acetyl-N-Methionine (2) for their healing and stimulating properties.

A combination of estrongen hormone and the amino acid, methionine, are synergistic in reducing the excessive secretion of the sebaceous appendages (2). The formulation appearing below rapidly dries and heals the papular-pustular formation, which is observed at the mouth of the pilosebaceous apparatus. This formula has been found to be clinically effective under our supervision. Seventy percent of the male patients are favorably affected; however, additional adjuvant measures must be included, as hygienic and dietary routines. A formulation that is useful in my practice is:

	Parts
Neutracolor	2.00
Estradiol	0.32
Resorcin	2.00
DL-Acetyl-Methionine	1.00
Colloidal sulfur	5.00
Propylene glycol	6.00
Liquid powder base	
q.s.a.d.	100.00

4) Foundation therapeutic lotion: Contains same formula as foundation acne lotion; however, resorcin is added, which is more keratolytic and exfoliating than the foundation lotion. Both preparations are marketed in various skin tinted shades and can be made lighter by adding titanium dioxide, and darker by adding neutracolor. If strong exfoliation is desired, betanaphthol—2 to 5%, or salicylic acid—1 to 5% can be added to the above formulations.

5) Astringent antiseptic lotion: Contains—	
Hexachlorophene	1%
Zinc sulfocarbolate	3%
Propylene glycol	6%
Ethyl alcohol	100.0

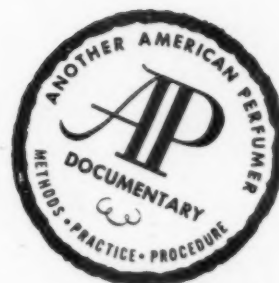
The use of hexachlorophene—1% is recommended, because at the present time no definite evidence of allergic sensitivity has been reported in the medical literature.

The oral use of water soluble Vitamin A—75 thousand units daily in three divided doses has, in the hands of some dermatologists, been found effective in returning abnormal keratinization to normal activity. Proof has not been established therapeutically.

Mild toilet soap containing hexachlorophene or biothional 1% base, also is helpful in reducing the activity of the staphylococcus aureus which is found in abundance in pustular acne.

Additional soaps have been suggested which may contain sulfur, resorcin and salicylic acid. Their effect is to produce mild exfoliation. However, frequently, excessive drying results, and the soap must be used on alternate days. More recently, the use of an abrasive cleaner has been recommended which may contain hexachlorophene 1% with various grades of mesh of the aluminum silicates.

ALLANTOIN



Extensive use of Allantoin as a most effective adjunct in cosmetic preparations has exhibited its reparative and cleansing actions as well as skin softening properties.

S. B. MECCA*

Allantoin, chemically identified as the diureide of glyoxylic acid or 6-ureido hydantoin has been employed effectively since approximately 1912 when Macalister (1) identified it as the active principle of the ancient "wound-wort," "Saracens consound," or "comfrey root." Years later Robinson (2) traced the cleansing and healing characteristics of maggots in wounds, also to the presence of allantoin. A complete review of its history and use has been presented in a previous paper (3).

Throughout the years, the valuable cell-proliferant action of allantoin has been widely utilized in various pharmaceutical preparations to heal all types of cuts, burns, wounds, ulcers, etc. By chemically debriding necrotic tissue allantoin cleanses the site while stimulating granulation and epithelization to repair and normalize the affected area.

Current research, with the aid of modern scientific techniques, such as the Schwartz Patch Test, Draize Technique and Repeat Insult Test, has shown allantoin to be non-irritating, non-toxic and non-allergenic. These findings coupled with the fact that no reports of untoward reaction have appeared in literature (for some 50 years), led to the present extensive use of allantoin as a most effective adjunct in cosmetic and dermatological preparations wherever its reparative and cleansing action as well as skin softening properties are desired.

Flesch (4) demonstrated that allantoin (in 0.2% solution) is an effective protein dispersant, denaturizing hardened horny (callus) tissue, even psoriatic scales. As a result of this study Clyman (5) Samitz (6) and Bleiberg (7) studied an allantoin-tar lotion for the treatment of psoriasis in varying degrees of severity and longevity. They conclude that the keratolytic action of allantoin helps to remove the pathological scales while at the same time effectively soothing and healing the irritated underlying tissues and in most cases arresting completely the further formation of these scales.

It has also been indicated that allantoin has a detoxifying and anti-irritant action in that it reduces the known irritant and toxic reactions of certain compounds such as sulfonamides (8), ammonia (9) and aluminum (10).

LeVan, et al (11), Kahan, et al (12) and Kaessler (13) report the use of 0.2% allantoin combined with hexa-

chlorophene and silicone in a cream lotion or talc for the effective treatment of diaper rash and similar eczematous irritations including its prophylactic application for such cases.

In the past year, a new group of compounds, the aluminum allantoinates, have been developed (14). Extensive clinical studies with aluminum chlorhydroxy allantoinate and aluminum dihydroxy allantoinate prove that they retain the attributes of allantoin plus the mild astringency of aluminum. Aluminum chlorhydroxy allantoinate also has a bacteriostatic action and deodorant effect. A brief description of each follows:

Aluminum chlorhydroxy allantoinate (complex), $\text{Al}(\text{OH})_3\text{.ClC}_4\text{H}_5\text{N}_3\text{O}_5$ is soluble in 1.7 % water (pH 4.7). Concentrations of 0.2 to 2% are used in after-shave and astringent body lotions, deodorant creams and lotions, acne preparations, etc. Clinical studies indicate that individuals prone to irritation or sensitization from the use of anti-perspirant-deodorant preparations are able to use them with comfort and freedom when 0.25% aluminum chlorhydroxy allantoinate is used as additive to the formulation (10).

Aluminum dihydroxy allantoinate, $\text{Al}(\text{OH})_3\text{.C}_4\text{H}_5\text{N}_3\text{O}_5$, is a true salt of allantoin, insoluble in water. Interestingly, it has both acid and alkali (ammonia) binding properties. Concentrations of 0.2 to 2% in an antiseptic cream or talc exert anti-irritant, mild antiperspirant, and prolonged healing action in the treatment of moist, weeping, eczematous lesions (diaper rash), decubitus and leg ulcers, etc. Hand creams containing 0.5 to 0.75% aluminum dihydroxy allantoinate effectively cleared up and controlled dermatitis venenata due to soap, water, alkali, or detergent irritation (10).

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Sulphur in Cosmetics and Dermato-Therapeutics

One of the oldest remedies which has been used in dermato-therapeutics. It is added only for its therapeutic effect and not for its immediate cosmetic action.

T. E. NEESBY *

One of the oldest remedies which has been used in dermato-therapeutics is elemental sulfur (7). It has been added in powdered form to lotions, soaps, powders, ointments, etc. Sulfur is added only for its therapeutic effect and *not* for its immediate cosmetic action.

The specific field of application for sulfur is acne vulgaris, also known as pimples, and its allied conditions: seborrhea with blackheads (comedones) and certain infections of the skin. Sulfur and sulfur products have also found applications in preparations for the scalp (soaps, lotions) against dandruff (pityriasis), seborrhea and different allied conditions (39).

During the last 2000 years a great number of recipes with sulfur have been used. It would be impossible to give in a few pages the history of sulfur preparations. The two main applications for sulfur cosmetics are acne and dandruff; both will often go spontaneously into re-

mission. Even though practically every adult has had or will have dandruff, often several times during life, the size of the potential market may easily be overestimated.

Persons suffering from acne are mostly adolescents, and the affliction often vacillates with the seasons, diminishing during spring and being most severe during the winter months (20, 22). The potential market for acne preparations is somewhat seasonal and advertising must be planned with these facts in mind.

Skin Penetration

All living cells are surrounded by a membrane that protects the inner plasma. Most higher organisms have in addition different other barriers which are semipermeable. Thus, there are the blood-brain barrier and the skin barrier. Important functions for the human organism are located in these barriers.

*Schieffelin and Co., Research and Development Dept., New York



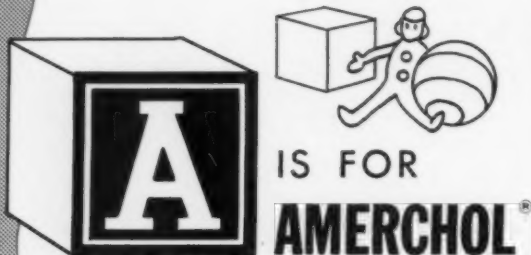
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The healthy human skin is a selective screen that serves the following purposes:

- It acts as a barrier for the penetration of many compounds especially high molecular compounds. (mol. w. >400) (16, 37, 24).
- It counteracts loss of water and important organic matter (23).
- An exchange of gases (oxygen) takes place through the skin (30).

The skin will permit the penetration of small molecules especially such that are lipid-soluble for example, chloroform, carbon tetrachloride, methyl salicylate and many other essential or ethereal oils.

This means that a number of therapeutic compounds can be absorbed through the skin and applied in ointments and lotions (12, 32, 33).

The fatty parts of the ointments and creams are not absorbed by the skin (2, 3, 5). Recent investigations of Jacobi especially illustrate this fact (14).

By the use of radioactive inorganic sulfur in a Vaseline® ointment, it has been demonstrated that sulfur penetration takes place (34, 36). Externally applied polythionates will also give rise to a rapid penetration of sulfur compounds (25, 26).

The possibility for a local effect of the penetrating sulfur compound on the multiplying cells of the epidermis is indicated. An autoradiograph of a section of skin after application of polythionate (marked with S35) shows heavy concentration in the stratum corneum.

The penetration of polythionates into the skin of rats has been studied biochemically and by autoradiography (in rats) (25, 26). An enlargement of such an autoradiograph is shown in Figs. 1 and 2 and can be compared with an enlargement of a histological preparation of rat skin, showing the penetration through the stratum corneum with the corium most heavily active. A corresponding section of the skin which was washed in running water for about ten minutes before embedding in paraffin showed practically no presence of radioactivity. Very little sulfur has been incorporated as organically bound sulfur in the 1½ hours during which time the skin was exposed to polythionate solution. It has been shown that the sulfur does become bound by the cells during longer interactions (34).

Pharmacology of Sulfur and Sulfur Compounds

Elemental sulfur is practically insoluble in pure water at ordinary temperature; boiling water containing alkali causes hydrolysis to occur and hydrogen sulfide, sulfites and/or sulfur dioxide, sulfates or thiosulfate will be formed. Powdered sulfur generally smells of "sulfur" indicating the formation of volatile compounds.

Since ancient times sulfur has been burned for fumigation. Sulfur dioxide is an irritant and cytotoxic, more specifically it is bactericidal and fungicidal. Hydrogen sulfide is toxic to man at concentrations of 0.005 per cent in the air. However, toxic levels are only accidentally experienced since the smell of H₂S is sufficiently obnoxious to be unbearable at lower concentrations. H₂S is not bactericidal nor fungicidal (20). Many organic sulfides have also a repelling smell and but few have any cosmetic use. Mercapto acetic acid is the exception. It is used in hair waving lotions.

The dermatologically important group of polythionates are characterized by inherent lability and instability. Chemically these compounds distinguish themselves as being oxidants, i.e., tetra and pentathionates. By this is meant that they will oxidize sulphydryl groups to disulfides.

This function may be the reason why tetrathionates have been found to be nephrotoxic when injected I. V. (6, 10). The cytotoxic effect could be due to a blocking of free SH groups. The specific fungicidal and bactericidal activity of polythionate is partially dependent upon the pH of the medium in which they are tested. Unpublished investigations of the author have shown that, for example, against *Staphylococcus aureus* the polythionates are only bactericidal at levels lower than pH 4.00. Detailed studies of Pedersen, *et al.*, have demonstrated growth inhibition between pH 4.9 and 5.6 (21). These investigators are of the opinion that at lower pH no specific bactericidal effect can be ascribed to the anion (polythionate). The author has, however, found that in ordinary media without polythionate a pH 3 is necessary for a bactericidal effect while in the presence of polythionates the bactericidal effect could be demonstrated up to a pH of 4.00.

Elemental sulfur as well as polythionates react fast with living tissue. Sulfur when brought in contact with minced tissue such as liver immediately gives rise to an evolution of hydrogen sulfide, presumably through the donation of hydrogen from the enzymatic systems (12).

Several enzyme systems are activated by reducing conditions while progressive oxidation inhibit enzymatic activity. Thus, certain proteolytic tissue enzymes as well as arginase are activated by reducing agents (1).

An elevated arginase content has been demonstrated in psoriasis (31). Regulation of excessive cell proliferation by polythionate may therefore have an explanation in the oxidation action of the polythionates although it has not been proven that the polythionates penetrate intact.

Dermatological Use of Sulfur and Some Sulfur Compounds

Obviously, the pharmacology of sulfur compounds varies with the constitution of the compound. Nevertheless, when we talk about "sulfur effect" in dermatology this entity is generally understood to encompass a number of therapeutic actions which together form a characteristic and well-known picture; "the effect of sulfur on the skin." The main characteristic of this picture is that of the slow but beneficial dermatological effect of powdered sulfur when externally applied to the skin or scalp.

Elemental sulfur when prescribed by the dermatologist is used for instance, as the U. S. P. Sulfur Ointment: 15 per cent precipitated sulfur in lanolin and petrolatum.

This preparation is used, for example, in the therapy of ring worm infections and pediculosis, but also in acne, pityriasis, seborrhea, etc. A perusal of the standard ready prepared sulfur-containing products shows that quite often sulfur is used together with other compounds like salicylic acid, resorcinol, etc. These mixtures are likewise used in the treatment of seborrhea, exzema, dermatitis, lupus erythromatosus, psoriasis and others.

The beneficial effect of elemental sulfur when applied to the skin may be due to the formation of soluble compounds (22, 17, 18, 19, 31, 40, 42). The effect of the oxyacids is especially well known. Formation of lipid-soluble sulfur-compounds could take place and probably also some hydrogen polysulfides. The presence of oxygen, water and amino groups of skin proteins could give rise to the formation of thiodiamines which compounds may constitute a way for the transportation of

sulfur through the skin barrier. It is a fact that sulfur applied to the skin emits a sulfur-like odor. There are, according to the chemistry of sulfur, two ways the deposited sulfur can act, namely, by forming sulfides or oxyacids (11, 20). Practically all sulfur compounds except sulfates are rather labile in the presence of water, oxygen and proteinaceous matter. Therefore, the direction of pharmaco-dynamic action exerted by an elemental sulfur preparation depends mainly upon the character of the vehicle. Obviously, if there are free acids present like salicylic, a favorable condition for the existence of polythionic acid is present. However, if the ointment or lotion base contains ZnO, a considerable alkaline buffering effect could be expected. Under these conditions very little chance exists for the formation of great amounts of polythionates.

Since one of the supposed beneficial effects of the polythionic acid is its tanning action, resorcinol may be added to nonacidic combinations.

In human medicine developments in the dermatotherapeutic use of sulfur followed the general trend in science. Thus, with the revelations of the "wonders" of colloidal chemistry, attempts were made to apply colloidal sulfur in human therapy. Colloidal sulfur is very easy to make in the laboratory. Anyone can dissolve sulfur in alcohol, dilute with water and get a white colloidal solution. One can also make the so-called "Wackenroder's" solution from H₂S and SO₂ (9). However, both products are unstable and therefore unfit for manufacturing. Different stabilizers, e. g., organic colloidal materials have to be added (29). However, the final product does not generally contain true colloidal sulfur, the particle size falling outside the range of true colloids (9).

Often when large amounts of stabilizers have been used, no immediate therapeutic effects have been found from topical application.

In order to make the sulfur easily available to the skin, organic sulfur compounds have been tried in dermatotherapy. These compounds are insoluble in water but soluble in alcohol and therefore especially well suited for lotions, hair tonics, etc. However, some organic sulfur compounds have shown allergenic and sensitizing properties.

The factices, i. e., reaction products between sulfur and unsaturated oils have also been tried. The effect of such compounds was quite good. Alcoholic solutions could be made from sulfurated castor oil products.

These products had certain hair grooming properties. Their inherent drawback was the obnoxious sulfur odor which appeared after application. As a result, most of these preparations were discontinued.

Colloidal sulfur preparations can, on the other hand, be quite effective in dermatological respects. A 5 per cent solution of true hydrophilic sulfur, a purified Wackenroder's solution with a little wetting agent added can have an action which surpasses more concentrated sulfur ointments. Such preparations are furthermore hypo-allergenic and show only a rare sulfur sensitivity reaction which may be experienced by persons with very light complexions. One of these commercial products is dated because it is light sensitive (24).

The comparatively rapid and beneficial effects of true hydrophilic sulfur solution have been speculated to be due to the content of polythionic acids (9, 11, 20, 21, 38). However, since no truly hydrophilic sulfur solution has been made free of polythionic acids, it will be difficult to substantiate this thesis. The sulfur micelles supposedly consist of either sulfur or a high molecular hydrogen polysulfide protected by polythionic acids. The micelles may also be considered built up of high molecular polythionates (9).

Whatever the way these complexes are constituted they are thermodynamically unstable; conversion into crystalline sulfur releases heat.

The special properties of, for example, pentathionic acid, is illustrated by the solubility of sulfur in it. Thus, Young made a strongly yellow solution consisting of sulfur in polythionic acid (43). If this product is diluted with alcohol, it can be painted onto the skin, and it will on drying form a yellow plastic coat. Unfortunately, the solution is unstable and no marketable preparation has been produced according to his procedure. Colloidal sulfur can also be made by melting sulfur and sugar or carbowaxes together. Not much is known of such preparations.

The polythionates have shown promise because of the cleanliness which characterizes the application of many such preparations. An aqueous solution or a dilute alcoholic solution containing acid sodium polythionate applied to the skin and scalp has been demonstrated to have an excellent effect (7, 8, 15, 21). After drying an invisible but active material is left on the skin.

The advantage, from a therapeutic point, of an invisible product on the skin may become insignificant when the preparation is provided with flesh colored pigments such as in cosmetics. Here insoluble sulfur compounds, such as finely dispersed sulfur or quaternary ammonium polythionates may be advantageous (28).

In vitro even in great dilution, polythionic acids precipitate proteins. In this respect the effect resembles that of resorcinol and resorcinol monoacetate. In many commercial preparations sulfur is used together with resorcinol. In alkaline or neutral media polythionates do not precipitate proteins, nor do they have any bactericidal-bacteriostatic effect, because they rapidly decompose. They then tend to restore acidic conditions in the process of liberating hydrogen ions. Elemental sulfur likewise will absorb hydroxyl ions by interaction with alkaline materials, forming thiosulfates, sulfides and under favorable conditions, polysulfides.

As yet unpublished investigations of the author and co-workers have shown what finely dispersed sulfur penetrates faster than elemental sulfur ointment, while polythionates penetrate still faster.

Another element from group VI, namely, selenium has found use against dandruff. It is combined with sulfur in a suspension shampoo (Selsun®). A rapid penetration has been demonstrated by analysis of the urine of persons who have used it on the scalp. Recent investigations have shown that selenium furthers keratinization (4). (A British product containing selenium sulfide also contains bithionol—Editor).

Hypersecretion of sebaceous matter from the glands can also be brought down to a more normal level by externally applied sulfur (20).

Often the effect of elementary sulfur on the skin is accompanied by some redness, dryness and cracking, but these signs of excessive therapeutic effect are mostly considered as an indication of proper pharmacodynamic actions (20, 38).

No real allergic reactions seem to have been registered against pure elemental sulfur (20).

Desquamation or scaling of the skin which is seen by intensive local application of sulfur may be due to the sudden regulation of the proliferation of cells indicating return to more normal rate of metabolism and multiplication.

The keratolytic and keratoplastic qualities of sulfur which have been mentioned so often are in their extreme form due to the reducing properties which sulfur acquires in alkaline media. These are, therefore, not too significant in ordinary cosmetic preparations, but are used in depilatory and hairwaving preparations.

It is a question whether the effect of polythionate is strong enough to account for the action of hydrophilic colloidal sulfur. Both colloidal sulfur and polythionic acid have been used in anywhere from 2 to 5 per cent solution with comparable effect.

It would be interesting to try the topical effect of hydrogen polysulfide, however, these products are rather unstable and have an obnoxious odor.

As mentioned, there is no doubt that sulfur does penetrate the skin and with great rapidity in cases of seborrhea (34). Polythionates when applied to the skin will rapidly penetrate. When applied in a small cup to the skin of rats, 8 per cent of the deposited polythionate sulfur was found in the liver after one hour (26).

The penetrating sulfur compound may affect the metabolic processes of multiplying or secreting cells and thereby regulate a too prolific growth or secretion of sebum. Several explanations are possible such as influencing the Redox potential by the oxidizing effect of polythionates on sulphydryl groups. This of course depends upon whether the polythioanions penetrate through the unbroken skin barrier.

Another way to influence the metabolism would be to depress the oxidative process by the interference of H₂S which the sulfur compound may release systematically.

Elemental sulfur and acid polythionates tend to restore or fortify the so-called acid mantle of the skin, thereby making it unfit as a residence for many pathogenic bacteria. Thus, the fungicidal-fungistatic and bacteriocidal-bacteriostatic effect of unbuffered preparations will reduce the number of viable micro-organisms on and in the skin (38). Deep-seated boils are therefore not affected by external sulfur medications (20).

The exact manner of conversion of sulfur on and in the skin has still a few unexplained steps.

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ARE TOPICAL VITAMINS UNDERESTIMATED?

Research alone can provide the answer, but question is clear that vitamins may turn out to be of value in lessening the degree of wrinkling in the aged.

BARCLAY NEWMAN

and

B. T. PALERMO*

Eleven vitamins are known to be indispensable to human beings throughout life: vitamins A, C, D, and K, plus seven B vitamins—B₁ (thiamine), B₂ (pyridoxine), B₃ (cyanocobalamin), riboflavin, niacin (or niacinamide), folic acid, and pantothenic acid (calcium pantothenate). Although the majority of common skin disorders are not significantly connected with nutritional deficiencies,¹ general undernutrition as well as numerous vitamin deficiencies result in abnormalities of the skin. Signs of deficiencies of certain vitamins are often more readily detected in the skin than in other tissues. Severe, pro-

longed inadequacy of vitamin A results in abnormally dry skin, papular eruptions, horny thickening of hair follicles, and keratinization of palms, soles . . . Seborrheic dermatitis (oily, scaly disorder of skin, especially of the face, often with itching) may be associated with deficiency of riboflavin or vitamin B₂, as may cheilosis, or cracking and scaling at angles of mouth and on lips. In severe deficiency of niacin, the skin is reddened and inflamed, with blister-like eruptions, cracking, weeping, ulcerations, and crusting; the skin may undergo atrophy and pigmentation associated with photosensitivity. In vitamin C deficiency, capillary walls give way, and many bleeding points

may be seen in the skin . . . Whereas certain avitaminoses have marked effects on the skin, as part of the picture of general undernutrition the skin ultimately suffers damage from any vitamin deficiency that is severe and prolonged. Excessive wrinkling of the skin may be, among other things, a side effect of protracted intense stress. Such stress multiplies vitamin requirements.

The Problems of Aging Skins

Adequate nutrition aids in countering damage due to great and lasting stress. Hence, a question can logically be suggested: Is it not possible that topical vitamins might

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turn out to be of value in lessening the degree of excessive wrinkling and certain other concomitants of aging? Research alone can provide the answer.

Vitamins would seem to have special significance in the prophylaxis and therapy of skin disorders in the higher decades of life. Rattner, in the standard treatise, *Geriatric Medicine*, states:

"The newer knowledge of the effects of vitamins on the skin suggests that they may be helpful in preventing certain changes peculiar to old skins."²⁶

Possibly, vitamin A administration may help to retard such degenerative changes as dry skin and scaly dermatoses.²⁶ Further: "the indication for vitamin-B complex lies in the fact that, in many elderly persons, the diet is deficient because of poor teeth or dentures or digestive disturbances, and it may be, as is so often claimed, that low-grade vitamin-B deficiencies are not uncommon among the elderly." Certain cases of eczema in oldsters may be due to undernutrition.²⁶

Here noteworthy is Lorincz's description of skin changes associated with general undernutrition:

"In general undernutrition, as occurs in genuine starvation or severe

gastro-intestinal diseases, the skin shows vascular pallor, dryness, and reduced elasticity. In addition, melanosis, scaling, hemorrhagic phenomena, and increased susceptibility to many sorts of infections and irritations may develop."²⁷

Very similar changes are characteristic of senile skin.²⁸ Only future research can reveal whether prolonged high dosage therapy with oral and topical multi-vitamins can have generally favorable influence on such features of "old-aging."

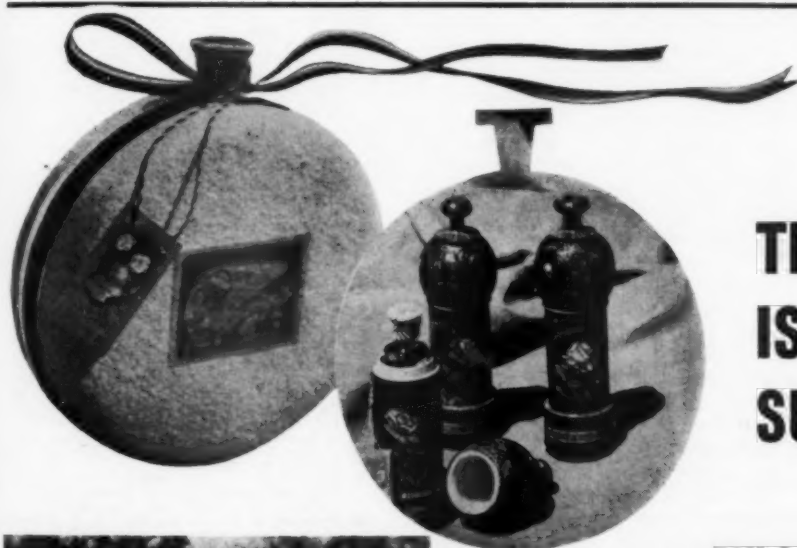
Additional considerations which may be of significance in geriatric dermatology are: (1) As age increases, the incidence of abnormalities conceivably causing localized vitamin deficiencies also rises; (2) The older the patient, the more likely it is that skin disorders associated with nutritional deficiency have had a lengthy period of development—and may be expected to respond relatively slowly to therapy, even if vitamins are provided in comparatively large doses; (3) Localized neurodermatitis increases in both frequency and intensity as the later decades are accumulated,¹⁷ and (4) Vitamins B₁ and B₂ have been repeatedly reported to exert markedly favorable influence in certain disorders of the nervous

system as well as of the skin.²¹⁻²³ Vitamin B₁₂ may even have a direct pharmacologic effect on nerves. And it is involved in nucleoprotein synthesis, a process of basic significance in exfoliative dermatoses that increase the need for steady replacement of cellular proteins lost by desquamation. Local changes which are due to the skin disorder may increase vitamin B₁₂ requirements in restricted areas.

Finally, niacin has been reported to have definite anticholesteremic effects.²⁶⁻²⁷ What will be the long-term results of high doses of these vitamins in countering arteriosclerosis? Would they thus eventually improve circulation to the skin, thus benefit skin lesions associated with impoverished circulation and conceivable localized vitamin deficiency? Clinical research alone can answer these questions. In the meantime, vitamins are indicated more and more extensively in dermatoses of older patients, so often deficient in these vital food factors.

Localized Deficiencies of Vitamins Conceivable

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disease, thrombosis, embolism, edema, prolonged pressure (as results in decubitus ulcer), overgrowth of connective tissue, scar formation, excessive fat deposit, various dermatoses . . . A localized deficiency of nutrients, including vitamins, may ensue. Oral or parenteral administration of vitamins in the doses used in dermatologic studies may then be inadequate. In such conditions, it might be necessary to administer vitamins topically as well as orally or parenterally. Recently, Wayne *et al.*¹⁸ reported that topical administration of vitamin B₆ in a bland cream base gave surprising results as follows:

"Skin levels of vitamin B₆ were studied in normal persons after topical vitamin B₆ was used with and without the addition of intramuscular vitamin B₆. Normal skin levels in 19 subjects ranged from 0 to 1.6 µg. per gram of skin. Five persons received local application of . . . vitamin B₆ . . . Six patients received the vitamin B₆ intramuscularly alone. Skin biopsy specimens were obtained after the areas from which the specimens were to be taken had been scrubbed three times. These were analyzed for vitamin B₆ levels. Five to thirty times as much vitamin B₆ was found accumulated in the skin after application of the cream alone as could be found when the vitamin was given intramuscularly alone. The parenteral form of vitamin B₆ in these experiments was not absorbed into the skin and did not alter the skin levels of vitamin B₆."

The Problem of Dosage and Type of Preparation

Massive doses of vitamins have been given orally or parenterally in the treatment of many skin disorders. Striking benefits have often been reported. In a few of the conditions where a deficiency does not exist, such beneficial use has been established and may be attributable to a pharmacologic type of action following massive doses. As suggested by the recent work of Wayne *et al.* (cited in the preceding paragraph), topical application of appropriate vitamin preparation may be expected to give a far higher vitamin concentration in the skin than could possibly be attained by systemic administration of the vitamin. New vistas may appear in the future if research discovers novel types of vehicles to enhance vita-

min absorption, special forms of highly absorbable vitamins, effective combinations of vitamin plus enzyme or steroid hormone. The implications of the reported favorable dermatotherapeutic results with vitamins in massive dosage would seem thought provoking, particularly in the light of the possibility of attaining still higher skin concentrations of a given vitamin by use of superior types of topical preparations which might be developed.

New Vitamin Preparations May Win Dermatotherapeutic Victories

Possible explanations of the reported variability of response to vitamins in dermatoses and in the effort to forestall certain concomitants of aging include the following: (1) Oral or parenteral administration may not provide an effective concentration of one or more vitamins in the skin. (2) Available topical preparations do not adequately promote vitamin absorption, and higher vitamin levels in the skin may be required for a pharmacotherapeutic effect. (3) Reports may have pertained to conditions in which vitamin therapy could have no confirmable value. (4) A certain percentage of cases of one dermatosis or another may be expected to involve nutritional deficiencies, which may not be of significance in other patients with the same skin disorder, or a different type of skin disorder with the same symptoms and signs. "Clinical experience teaches that pathological responses of the skin to widely varying stimuli may be identical." For example, a case of seborrheic dermatitis may be due to vitamin B₆ deficiency, or to riboflavin deficiency, although many cases may result from a "constitutional diathesis affecting the skin, an often inborn physiologic trait which usually can be controlled but not 'cured'."¹⁹ (5) Results of prolonged vitamin deficiency must sometimes be given a considerable length of time to respond. Far-advanced damage may be but slowly reversed. How many times have the potentially favorable therapeutic effects of vitamins in a given skin condition been underestimated—because of underestimation of the time required to gain maximal improvement from such therapy? . . .

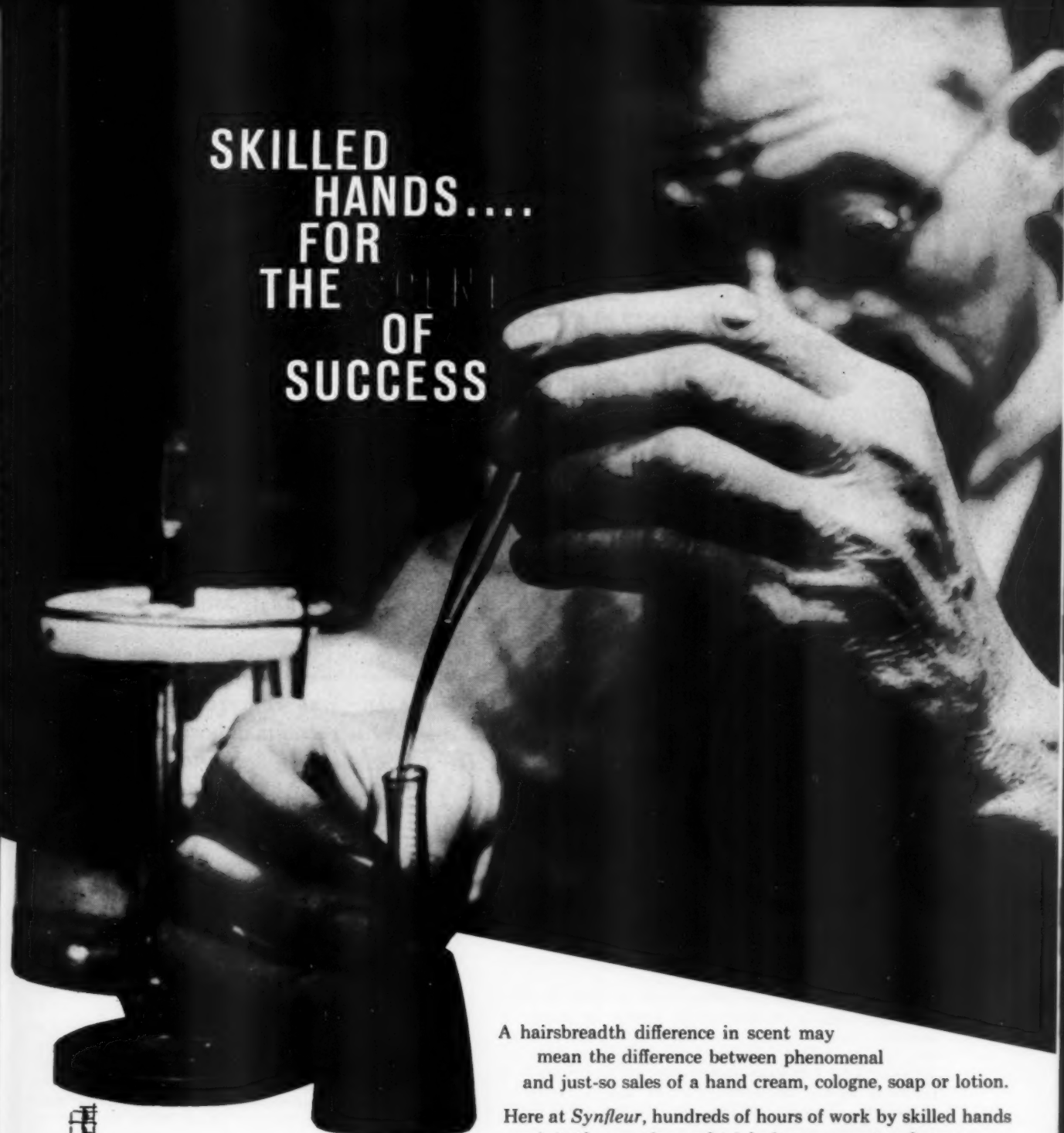
Perhaps the most important possibility is: New vitamin preparations still to be developed for topical

use may promote vitamin absorption to such an extent that novel and extraordinarily valuable pharmacologic as well as nutritional influences would be focused at the precise site of the lesions in the skin. The key to future success is to be wrought by research.

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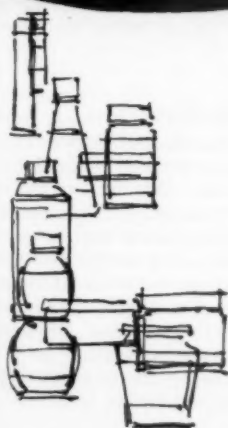


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TOPICAL CHEMICAL ANTIINFECTIVES

It appears actually impossible to devise any one representative method which would cover the whole range of circumstances under which antiseptics are used. Here is a discussion limited to chemical topical antiinfectives.

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Bacterial infections of the skin are subject to control by means of antiseptics applied topically, or of antibiotics applied systemically or topically, or both. Fungus infections cannot be treated, as a rule by means of systemic therapy, except for actinomycosis and sporotrichosis for which systemic treatments have been developed. The following discussion will be limited to chemical topical antiinfectives, and will not consider, therefore, either antibiotics or systemic chemotherapeutic agents.

Definitions

The term *antiseptic* meant originally a substance opposing sepsis by preventing or arresting the growth or action of microorganisms. Nowadays, it is used especially for agents applied to living tissue. More recently, the term *antiseptic* has acquired a precise legal connotation since it is referred to specifically in the Federal Food, Drug and Cosmetic Act as meaning the same as a germicide, except where its use involves prolonged contact with the body, as opposed to a temporary contact, e.g., in the case of a mouthwash, an eye bath, etc.

All terms construed with the suffix *-cide* imply capacity of killing; this would be true of terms such as *bactericide*, *microbicide*, or *fungicide*.

*Lehn and Fink Products Corp.

The suffix *-static* is used to describe an ability to prevent microbial growth without killing the microorganism. The suffix may be employed in general terms such as *bacteriostatic* or *fungistatic*.

The term *degermation* is intended to describe the reduction of the so-called resident bacterial skin flora by the action of certain antibacterial agents usually incorporated in soaps or detergents. *Degermation* is not synonymous with *disinfection* since, actually, the skin cannot be disinfected, i.e. freed from all of the bacteria present upon it.

Notes on Testing Methods

The methods prescribed by Ruehle and Brewer for the examination of antiseptics, and entitled "United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants" enjoyed, for some time, a quasi-official status, having originated with a governmental authority (1). They are still useful for a first screening of new preparations designed as antiseptics, i.e., prior to a more extensive clinical evaluation under the practical conditions of their intended application. However, the Food and Drug Administration no longer sponsors these methods; according to its present position, there exist no standard or official tests for the

evaluation of antiseptics, and no single *in vitro* test is considered sufficiently informative to serve as a criterion of presumptive performance under the conditions of practical use.

It appears actually impossible to devise any one representative method which would cover the whole range of circumstances under which antiseptics are used. Thus, obviously, the same criteria of performance should not be applied to an antiseptic mouth-wash as are applied to a first-aid antiseptic for use on wounds, abrasions, etc. More comprehensive information is elicited by a "profile evaluation" involving the combination of several different tests, with every test supplying an answer to a particular pertinent question.

To the extent that *Staphylococcus aureus* represents the most common cause of suppuration, coupled with marked resistance to both physical and chemical factors, its use as test-organism is logical in screening tests by means of one of the several applicable methods. However, for antiseptics applied to prevent infection through a break in the skin, an *in vivo* method such as that of Nungester and Kempf (2) or Sarber (3) will yield more relevant results.

Klarman, Wright and Shternov, (4) reported that their "semimicro" method furnishes more information about the performance of liquid antiseptics likely to come in contact with tissue fluids. One of the pragmatic features of this technique is control of the random sampling error inherent in methods which depend upon loop transfers from the "medication mixture" to the "sub-culture." In addition, its use considers the following premises:

1. The criterion of fitness of any antiseptic which is likely to come in contact with tissue fluids should be its demonstrated capacity for permanent suppression of bacterial activity under the conditions of use.
2. If an antiseptic which has prevented bacterial proliferation in a nutrient medium does not continue to prevent this upon subsequent contact with physiological material such as blood or serum, then its fitness for use as a pre-operative or wound antiseptic is open to question.

The procedure consists substantially of the following steps. A broth culture of *Staphylococcus aureus* is exposed to the action of the antiseptic for ten minutes, at room temperature. The reaction is stopped by dilution with about forty times the original volume of blood broth. The total mixture is incubated, and the results are read after 96 hours.

While the so-called degerming agents are not, strictly speaking, skin "antiseptics," the *in vivo* testing method developed for the evaluation of degerming agents furnishes comparative information about their presumptive practical performance. This method has been devised by Price, and is known as the "serial basin test" (5); later modifications (6,7) were suggested in order to simplify the procedure. The method involves, as its implied premise, the recognition of the fact that the skin cannot be "disinfected" in the true sense of this term, but that it is possible to reduce its "resident", potentially pathogenic bacterial flora, as may be required for reasons of safety, e.g. in surgical practice. The need for this reduction is indicated for the operating surgeon and assisting personnel to prevent the transfer of hand-borne pathogens into the surgical wound; it is indicated also in the case of the surgical patient whose skin should be "degermed" to the lowest possible level at the site at which the surface is to be broken.

Other things being equal the degerming agent is the more valuable, the more it is capable of depressing the

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resident bacterial count.

There are a number of published references to "tissue-toxicity", in connection with the practical evaluation of antiseptics. Although various pertinent testing methods have been suggested (8), it is held that the problem itself is not necessarily of primary importance with respect to the purpose for which an antiseptic is applied. Incidentally, some of the results obtained by one or another of these methods do not permit of a rational, practical utilization which would serve as the basis of a comparative evaluation of antiseptics.

This is not to say that, other things being equal, an antiseptic with lower tissue toxicity should not be given preference over a more toxic one; however, such an axiomatic statement is predicated upon the availability of a testing procedure which would be more representative of the conditions of actual usage than the test methods published to date. As matters stand now, one might even concede the possibility of an antiseptic injuring superficial tissue, or inactivating some leucocytes present locally, so long as such action is merely of a temporary character, while at the same time implying effective control of the infectious agent i.e., the prevention of its penetration to a depth where it could not be reached by prompt application of the antiseptic.

Parenthetically speaking, the problem of "tissue-toxicity" appears to be of considerably greater importance in the area of chemotherapy than in that of antiseptics.

Alcohols

One of the oldest and most popular bactericidal agents is ethyl alcohol (9,10,11,12); n-propyl and isopropyl alcohols exhibit comparable antibacterial efficacy when applied to the unbroken skin. The *in vitro* microbicidal action of ethyl and isopropyl alcohols is the subject of several publications (13,14,15). Ethyl alcohol is employed as a germicide most frequently in 70 per cent dilution by weight (78 per cent by volume).

In the homologous series of primary normal alcohols, the bactericidal effectiveness against *Staphylococcus aureus* increases with increasing molecular weight (from ethyl to octyl alcohol) (9). Primary alcohols with six to sixteen carbon atoms display an inhibitory action upon *Mycobacterium tuberculosis*, also upon *Trichophyton rosaceum* but not upon *Staphylococcus aureus* (16).

Neither alcohol nor alcoholic tinctures are suitable for use on areas of broken or fissured skin because of their irritant action.

Iodine

Of all halogens, iodine has held and even expanded its position in the field of antiseptics. Iodine is a highly reactive substance which combines with proteins partly by chemical reaction, partly by adsorption.

As a bactericidal antiseptic, iodine is used most frequently in the form of a 2 per cent tincture (with 2.4 per cent of sodium iodide), less so as an aqueous solution; stronger iodine preparations are employed occasionally for preoperative antiseptics. Iodine tinctures within the range of 2 to 7 per cent of iodine reduce the bacterial count of the skin by 97.5 to 100 per cent, as determined by the "serial basin test"; in this respect they appear to be markedly superior to the other antiseptics tested (17).

Iodophors are combinations of iodine with suitable solubilizing organic compounds (usually non-ionic surfactants) from which the iodine is released gradually to act as an antimicrobial agent (18). Iodine has been solubilized also by a cationic surfactant with formulation of a complex said to be comparatively bland for the skin and mucous membranes (19).

Mercurials and Other Metal Compounds

Mercuric chloride is one of the earliest antibacterial agents known. Ammoniated mercury, also mercuric oxide enter into the composition of several therapeutic preparations.

As to organic mercurials, much of the published information on their subject requires revision owing to lack of distinction between the bacteriostatic and the bactericidal action of the compounds studied. Pathogenic microorganisms in a state of bacteriostasis induced by mercurials have been found to retain their potential for infection (2,3,12,20). Blood is capable of reversing the inhibitory action of mercurials even after a prolonged contact (21,22).

Tinctures of organo-mercurials contain as the solvent usually a mixture of alcohol, acetone and water. Unlike their aqueous solutions, the tinctures are bactericidal *in vitro*; however, the solvent alone exhibits a significant effectiveness in this respect (23). The presumptive usefulness of several tinctures of organo-mercurials for preoperative application has been evaluated by Price (17).

Following are some of the more important organic mercurials: phenylmercuric nitrate and borate, merbromin (Mercurochrome), thimerosal (Merthiolate), mercocresol (Mercresin), nitromersol (Metaphen) and acetomerocetol (Merbak).

Several silver compounds are employed for antiseptic purposes. Silver nitrate is used for routine prophylactic instillation into the eyes of newborn infants. Silver picrate used to enjoy some favor in the treatment of trichomonal and gonorrheal vaginitis. A number of colloidal silver preparations continue in moderate use.

Phenolic Compounds

In the several different series of homologous phenol derivatives studied, certain regularities were found which correlate the weights and structures of substituting radicals with the antimicrobial performance of the phenolic compounds (24). Among other things, a "quasi-specific" effect has been observed which connects the molecular weight and structure of certain phenol derivatives with their microbicidal action upon particular groups of pathogens (25).

Among the more important phenol and polyphenol derivatives entering into the composition of antiseptic formulations are thymol, chlorothymol, amyl-*m*-cresol, *p*-chloro-*m*-xylenol, *o*-phenylphenol and hexylresorcinol.

A somewhat special position is occupied by substituted bis-phenol methane and sulfide derivatives. In this group belong hexachlorophene and bithionol. They are used mostly as additives to soaps or soapless detergents which thereby acquire the capacity of reducing the bacterial skin flora to a small fraction of its original, following routine use of such soaps or detergents (26).

8-Hydroxyquinoline used by itself or as a salt (sulfate, benzoate) is the active ingredient of some antiseptics whose action is inhibitory rather than microbicidal (27). Several halogen derivatives of 8-hydroxyquinoline have a record of therapeutic efficacy in the treatment of pyodermas and of dermatophytoses; among them are iodochlorhydroxyquin (Vioform; 5-chloro-7-iodo-8-quinolinol), diiodohydroxyquin (Diiodoquin; 5,7-diiodo-8-quinolinol), chlorquinaldol (Sterosan; 2-methyl-5,7-dichloro-8-quinolinol) and others (28,29,30).

Quarternary Ammonium Compounds

Although numerous quarternary ammonium salts were prepared and investigated over a period of time, only a comparatively small number are employed as antibacterial agents in general, or as topical antiseptics, in par-

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ticular. Among the more important are benzalkonium chloride, benzethonium chloride, cetyl pyridinium chloride and cetyl trimethyl ammonium bromide. When used for strictly antiseptic purposes, e.g. for the control of skin bacteria at the operative site, the "quats" are more likely to render satisfactory service if applied in the form of tinctures (diluted e.g. with 50 per cent alcohol—10 per cent acetone) rather than in aqueous solution. This conclusion is based upon the results of the "serial basin test," as employed in a comparative evaluation of the "degerming" effectiveness of several hospital antiseptics studied (17).

Carbamic Acid and Urea Derivatives

In an investigation correlating chemical structure with *in vitro* antibacterial and antifungal activity, it was found that within the categories of dithiocarbamates, and thiuram disulfides, the methyl and ethyl compounds were the most active while the higher alkyl derivatives were comparatively inactive (31).

Tetramethylthiuram disulfide (TMTD) was the most active of the compounds tested against pathogenic fungi as well as against bacteria, the gram-positive staphylococci showing a markedly greater susceptibility than the gram-negative pseudomonads and coli bacilli. Incorporated in soap, TMTD imparts to it a degerming efficiency comparable or superior to hexachlorophene (32).

A systematic investigation of a large number of urea and thiourea derivatives uncovered several strongly bacteriostatic compounds of which 3,4,4'-trichlorocarbaniide (TCC) is an example (33). It, too, is employed as a soap additive for its effective skin "degerming" action, sometimes in combination with other antimicrobial additives.

Hibitane is 1,6-di-4'-chlorophenyl diguanidohexane. It has been formulated with a cream to reduce the bacterial flora of the hands (34). It is also suitable for preoperative use in the form of a tincture (35).

Nitrofurantoin Derivatives

Of the numerous nitrofurans prepared and tested, several have achieved practical importance (36,37,38). Among them is 5-nitro-2-furaldehyde semicarbazone (nitrofurazone, Furacin) which exhibits antibacterial action upon both gram-positive and gram-negative microorganisms. It is useful as a topical prophylactic and therapeutic agent in mixed infections common to contaminated wounds, burns and pyodermas, also in the management of purulent otitis and conjunctivitis.

Tricofuron (Furazolidone) is an antiprotozoan as well as an antibacterial agent. Nitrofurantoin (Furadantin) is a wide spectrum antibacterial agent which may be administered orally.

Dyes

The actions of dyes is bacteriostatic rather than bactericidal in character. The inhibitory action of basic dyes (e.g. triphenylmethane or acridine derivatives) is attributed to the tendency of their basic ions to form non-ionizing or feebly ionizing complexes with the acidic groups of some cellular constituents; in the case of acid dyes (e.g. acid fuchsin), it is the acidic ion which is presumed to react with some basic receptor forming a different type of non-dissociating complex (39). These reactions are favored respectively by high and low pH values of the environment; i.e. bacteria become increasingly sensitive to basic dyes as the pH is increased, and to acid dyes as it is decreased.

At one time, the organic dyes enjoyed considerable practical importance. Some are still in use today. Among

the more important are: Brilliant Green (bis-(*p*-diethylamine) triphenyl carbinol anhydride), Gentian Violet (hexamethyl-pararosanine hydrochloride), Methylene Blue (methylthionine chloride), Acriflavine (3,6-diamino-10-methylacridinium chloride), Proflavine (2,8-diamino-acridinium sulfate) and Mallophone (Pyridium; 2,6-diamino-3-phenylazo-pyridine hydrochloride).

Miscellaneous

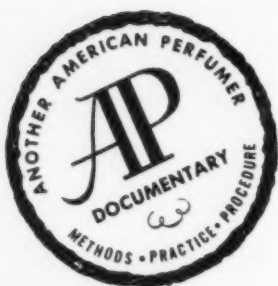
In recent years, preparations based upon low molecular aliphatic acids and their salts have gained importance as topical antifungals in the treatment of mycoses (40,41,42,43). Of the fatty acids, the propionic, caprylic and undecylenic acids are the most important; sodium propionate, sodium and copper caprylate and zinc undecylenate are formulated frequently in combination with the corresponding acids (44).

The salicyl and chlorosalicyl anilides are antifungal agents; they are used either by themselves or in combination with the fatty acids (45,46).

Asterol is 6-(β -diethylaminoethoxy)-2-dimethylamino-benzothiazole dihydrochloride. It is used in the treatment of mycotic infections, sometimes in combination with lithium bromide to facilitate penetration of the nail keratin (47,48).

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VITAMINS IN COSMETICS

The use of vitamins in cosmetics offers a challenge to both the dermatologists and the cosmetic chemists. The following article is both inspiring and thought provoking to the cosmetic industry.



By

E. DE RITTER, L. MAGID AND P. E. SLEEZER*

PART I

The Role of Topically Applied Vitamins.

The role of certain vitamins in maintaining the health and appearance of the skin is well known. Deficiencies of some of the vitamins lead to characteristic lesions of the skin as described below; in fact, the

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skin is often the first indicator of a dietary deficiency of one or more vitamins. Although the symptoms of such deficiency can normally be relieved by oral vitamin supplements, there is increasing evidence that for certain skin conditions topical application of vitamins can be an even more effective route of administration. Actually, it is possible to achieve a much higher local concentration of vitamins in the skin by topical appli-

cation than by oral dosage. In addition to the idea of supplying a nutrient substance to an epithelium believed to be deficient, consideration must also be given to the possibility that a vitamin may exert a local pharmacodynamic action on the skin, wholly or in part dependent on its chemical structure¹.

Neither the mechanism involved nor the exact result of a specific local pharmacodynamic action have been fully elucidated. This offers a challenge to dermatologists and cosmetic chemists, working together as a team. Undoubtedly, the findings of clinical work, now in progress, will result in even more extensive investigations of broad scope.

The penetration of the skin by vitamins has been demonstrated in animal or human experiments by a number of methods, including:

- 1—measurement of blood or urine levels
- 2—analysis of body tissues
- 3—observation of a characteristic reaction
- 4—histological examination
- 5—clinical examination

Specific examples of each of these methods will be described below for the individual vitamins to which they have been applied. The measurement of vitamin content of body tissues or fluids has been carried out by the usual physico-chemical methods and more recently by techniques involving radioactive tracing, which are particularly effective in proving percutaneous absorption. The role of the vehicle in absorption of active ingredients through the skin, although an important one, has been described in considerable detail^{2, 3} and will not be considered here.

The vitamins of interest to the cosmetic formulator are the following: Vitamin A, Vitamin D₂, Vitamin E, Biotin, Panthenol and Pyridoxine. The skin symptoms due to deficiency, the evidence for percutaneous absorption and the results of topical application will be described for each of these vitamins.

Vitamin A

The lesions of the skin due to vitamin A deficiency are characterized by excessive keratinization, a thickened horny layer, dryness and scaling. The conditions are termed keratosis and ichthyosis by dermatologists. The development of such conditions in the absence of any other evidence of vitamin A deficiency may be indicative of an underlying difficulty in transport of vitamin A to the skin. The topical application of vitamin A has been shown by Studer and Frey⁴ and by Sabella, Bern and Kahn⁵ to have an inhibiting effect on keratinization in the rat. A thickening of the stratum granulosum was observed with a resultant decrease in keratin formation and a thinner horny layer.

In 1934 Lohr⁶ introduced the local use of cod liver oil either alone or in an ointment as a wound dressing. Hardin⁷ published a comprehensive review in 1941 on the treatment of wounds and dermatological conditions with cod liver oil preparations, which yielded gratifying results. The disagreeable odor of fish oils, however, generally ruled out their use in cosmetic preparations. When in 1949 practically tasteless and odorless synthetic vitamin A became available, both therapeutic ointments and cosmetic preparations containing vitamin A came into general distribution.

The benefits derived from topical application of vitamin A have been reported by many authors, including Baer and Vogel⁸, Flesch⁹ and Reiss and Campbell¹⁰. A review of the use of vitamin A in dermatological and, especially, cosmetic applications has been published by Siemers and Sleezer¹¹. These au-

thors recommend concentrations of 1000 to 5000 units of vitamin A per gram for cosmetic purposes.

The absorption of vitamin A through the skin was demonstrated by Helmer and Jansen¹² and Eddy and Howell¹³ by the weight gain shown by Vitamin A deficient rats in response to topical application of fish liver oil. Sobel¹⁴ in similar experiments found local application of vitamin A to be about one-seventh as effective as oral dosage in promoting growth of deficient rats. This ratio was confirmed by De Ritter and Marusich¹⁵ by measurement of liver stores of vitamin A in the rat. Baer and Vogel⁸ attempted to correlate clinical improvement of dermatological conditions in humans after topical vitamin A with biophotometric readings. In some cases correlation was observed but the precision of the biophotometer is not adequate for this purpose. De Ritter and Jahns¹⁶ were unable to find an increase in human blood plasma level of vitamin A after application of a high concentration of the vitamin in a carbowax ointment. If absorption did occur, the rate was too slow to affect the blood level which tends to be maintained relatively constant through storage and mobilization from the liver.

Vitamin D₂

Because of the close association of vitamin D with vitamin A in fish oils, it has been common practice to include vitamin D in topical preparations containing vitamin A. The combination has been reported to stimulate epithelial growth^{17, 18} and promote healthy granulation and re-epithelization of burned areas¹⁹. The respective roles of the two vitamins in this regard have been discussed by Hardin⁷. Vitamin D is, of course, closely associated with skin since it is normally formed upon exposure of the skin to sunlight.

Efficient percutaneous absorption of vitamin D₂ (Calciferol) was reported by Schaefer et al.²⁰ on the basis of its effect in healing rickets in vitamin D deficient rats. De Ritter and Marusich¹⁵ have confirmed this absorption in similar rat tests, but the topical dose was found to be only about 7 percent as effective as oral dosage.

Vitamin E

Vitamin E as either alpha-tocopherol acetate or the unesterified form applied topically with or without associated oral dosage has been demonstrated to be useful in relieving severe itching and promoting healing of the skin.^{21, 22, 23, 24} Sobel¹⁴ has reported that vitamin E, in combination with vitamin A, produces increased storage of vitamin A in the rat when both are applied topically. The increased vitamin A storage in the presence of vitamin E has been described as a "sparing action" by the E. This may be either a type of synergism or possibly an antioxidant effect in the tissue by the biologically active vitamin E.

Biotin

One of the classic symptoms of biotin deficiency in various animal species is the development of dermatitic lesions^{25, 26}. These lesions develop in both rats and chicks fed diets rich in raw egg white due to their content of avidin which inactivates biotin. Observations in European clinics during World War II revealed frequent occurrence of severe dermatitic lesions, especially seborrheic dermatitis and Leiner's disease, particularly in young infants. Restricted

maternal diets, low in biotin, were implicated and healing of the lesions was observed following biotin therapy. An account of this and other instances of apparent biotin deficiency related to skin disorders has been published by Slezzer.²⁷ These clinical studies essentially involved oral or parenteral administration of biotin. While it does not necessarily follow that topical application of biotin will be equally efficacious, it is reasonable to consider the possibilities of such use. Advances in formulation of topical bases and unpredictable results with an active agent or the possible synergistic effects of active agents in a modern ointment base lend great weight to such development ideas.

Panthenol

When given orally, parenterally or topically, panthenol is converted in the body to pantothenic acid, a vitamin of the B-Complex. In experimental animals, one of the main effects of a deficiency of this vitamin is the development of lesions of the skin or hair.²⁸ Pfaltz²⁹ reported the local application of panthenol to give even more favorable results than oral dosage in treating achromotrichia of the black rat and alopecia of the mouse due to pantothenic acid deficiency. Burlet³⁰ found that panthenol applied to the skin of rats was absorbed and converted to pantothenic acid, the content of which increased in the skin both at the site of application and also in other locations. Urinary excretion of pantothenic acid by the rat was found by De Ritter and Marusich¹⁵ to represent 32 percent of a topical dose of panthenol as compared to 86 percent of an oral dose. In studies with guinea pigs, Mauchette³¹ found that panthenol aided greatly the regenerative abilities of the skin.

Although in humans a deficiency of pantothenic acid is not seen due to the widespread occurrence of this vitamin in foods, nevertheless, there is abundant evidence for the healing effect of panthenol applied to the skin. Numerous investigators in the United States^{32, 33, 34, 35, 36} have reported successful treatment of a variety of skin disorders with topical panthenol. The European literature contains even more abundant evidence of the benefits to be derived from topically applied panthenol.^{37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52} Cutaneous ulcerations, lupus erythematosus, burns, wounds, fissures and corneal lesions are among the disorders successfully treated by local application of panthenol.

In view of the evidence that pantothenic acid is essential for the integrity of tissues, including epidermis, it is not surprising that panthenol should be tried on hirsute skin. As noted above²⁹, the achromotrichia in black rats and alopecia in mice due to pantothenic acid deficiency can be cured by topically applied panthenol. Goldman and Mason³³ reported that of all the agents employed in their studies of human hair growth, panthenol and calcium pantothenate given orally seemed of some success in certain cases of congenital hair disturbance. Stangl³⁴ and Gsell⁵⁵ have claimed benefits to the hair due to panthenol given systemically or applied topically to humans with various disease conditions. Stangl³⁶ has demonstrated an increase in the pantothenic acid content of human hair after applying a solution of panthenol on the hair and scalp. Basal levels of 0.05 to 2.0 micrograms per gram of hair were increased after several months of panthenol treatment to 10.7 and 20 micrograms per gram. Similar increases were found by De Ritter and Schreiner³⁷. These observations are indicative of a useful role for panthenol in hair

preparations. In fact such products containing panthenol have been markedly successful in Europe.

Pyridoxine

Pyridoxine (vitamin B₆) deficiency in rats causes a specific, symmetrical dermatitis called acrodynia, which affects primarily the peripheral parts of the body.⁵⁸ Dogs⁵⁹ and pigs⁶⁰ also show a dermatitis as one of the signs of pyridoxine deficiency. Absorption of pyridoxine by the rat after topical application has been claimed by Schaefer et al.²⁰.

In human trials Schreiner et al.⁶¹ found that a cream containing 1 or 2 percent pyridoxine caused improvement in natural lesions of seborrheic dermatitis that had not responded when pyridoxine was given orally or parenterally. The cream alone did not have this effect and, after use of pyridoxine cream was discontinued, relapse occurred in most cases within a month. As another control test, the cream alone was applied to one side of the face and the cream with 1 percent pyridoxine to the other side. In those patients with dry type seborrhea, sharp differentiation could be made between the tests and the controls. Efferse⁶², on the other hand, could not confirm these observations.

Summarizing the status of pyridoxine in nutrition in the *Journal of the American Medical Association*, Vilter⁶³ states that "Vitamin B₆ is a very important nutrient that is essential for human beings." He further states that deficiency states occur only under unusual circumstances. Such deficiency states are manifested in the skin, mucous membranes and the central and peripheral nervous systems.

The relatively recent interest in a combination of vitamin B₆ and essential fatty acids has focused attention on such type products. In view of the apparent role of the essential fatty acids and vitamin B₆ in skin physiology, the cosmetic chemist and the dermatologist should seriously consider further investigation into the role of these two important nutrients in topical applications.

Conclusions

The results of both laboratory and clinical trials delineated above indicate a very useful role of topically applied vitamins in combatting various skin disorders. These conditions may not be due to a frankly deficient diet, but simply to a suboptimal level of one or more vitamins in the skin due to inadequate intake, improper functioning of metabolic systems, aging processes or actual disease states. Abnormal skin conditions may be aggravated further by exposure to the elements or to detergents commonly used on a regular basis. Topical application of vitamins can provide a local vitamin concentration in the skin considerably higher than will normally be attained by oral dosage. Penetration into the skin and/or absorption into the blood stream have been demonstrated for both fat-soluble and water-soluble vitamins. It remains to be learned how significant are the normal vitamin functions mediated via skin transfer.

Of equal significance may be the role of vitamins, applied topically, in exerting a localized pharmacodynamic action. Such cosmetic effects must be thoroughly studied. Clinical studies within this field should be assumed by the cosmetic industry. There are increasing evidences that progressively inclined cosmetic manufacturers are cognizant of this necessity for both fundamental and applied research within their expanding programs.

PART II

Incorporation of Vitamins in Cosmetics

In view of the relationship shown in the preceding section between the skin and vitamins, the incorporation of vitamins into cosmetic products appears to be justified at the present time. Vitamin A, vitamin D₂, vitamin E, panthenol and pyridoxine hydrochloride are incorporated in a number of well known commercial cosmetic and pharmaceutical products for their cosmetic and therapeutic effects. Among the already marketed preparations containing vitamins are the following forms, namely, creams, ointments, hair grooming liquids, lipsticks, aerosol hair sprays and lotions.

The incorporation of vitamins into cosmetic preparations requires a knowledge of the chemical and physical properties of the vitamins. The stability characteristics of the individual vitamins are well known and are standard information in pharmaceutical text and reference books.^{64, 65} The incorporation or inclusion of vitamins into cosmetic preparations is governed by the same general principles used in the addition of vitamins to pharmaceutical products. The literature abounds with studies of the stability and formulation of solid and liquid forms of vitamin preparations^{66, 67, 68, 69} which will be of value to the cosmetic chemist in his experimental formulations. There is no fundamental difference in the incorporation of vitamins into cosmetics as compared with pharmaceuticals. The many years of successful marketing of pharmaceutical vitamin dosage forms attests to the practicality of formulating vitamin products. The cosmetic chemist can generally prepare vitamin formulations in the usual manner with standard equipment, by maintaining the conditions for the optimum stability of the vitamins involved.

In formulating vitamin cosmetic preparations, one must be cognizant of the two classes of vitamins, namely, (1) the fat-soluble vitamins and (2) the water-soluble vitamins. The important members of the two classes of vitamins are shown below:

Fat-Soluble Vitamins	Water-Soluble Vitamins
Vitamin A	Thiamine Hydrochloride
Vitamin D ₂	Ascorbic Acid
Vitamin E	Riboflavin
Vitamin K	Niacinamide
	Panthenol
	Pyridoxine Hydrochloride
	Biotin
	Folic Acid
	Vitamin B ₁₂

Of current interest to the cosmetic formulator are the following vitamins: vitamin A, vitamin D₂, vitamin E, biotin, panthenol and pyridoxine hydrochloride. The essential fatty acids, as nutrients of importance in the function of the skin, may also be considered with the fat-soluble group.

Incorporation of Fat-Soluble Vitamins

The fat-soluble vitamins may be incorporated directly into the oil phase of cosmetic preparations or in the absence of an oil phase, into the water phase by means of suitable solubilizers, such as Tween 80. A ratio of 10 or 15 to 1 of the solubilizer to fat-soluble vitamin is required to make a clear, stable solution of the fat-soluble vitamin in water.

Vitamin A

The most useful and stable form of vitamin A for incorporation into cosmetic products is vitamin A

palmitate. Vitamin A palmitate is available as a yellow oil containing 1.3 or 1.8 million units of vitamin A per gram. It is insoluble in water, but is soluble in fats and oils. It can be solubilized in aqueous solutions by means of solubilizers such as Tween 80. The vitamin is not readily destroyed by heat, but is easily oxidized. Preparations containing vitamin A should be processed with adequate precautions to prevent oxidation. The formulations should be processed under an atmosphere of carbon dioxide or nitrogen. In the absence of air, vitamin A is not affected by moderate heat. Vitamin A is unstable in presence of rancid oils and may be unstable in creams containing stearic acid. Emulsifying agents used in creams and lotions should be free of oxidases and the perfumes should not contain peroxides. The addition of antioxidants to cosmetic preparations containing vitamin A in the oil phase is helpful in maintaining stability. Vitamin E in the unesterified form is preferred and is effective as an antioxidant for solutions of vitamin A in oil. In aqueous solutions, in the absence of an oil phase, antioxidants are also likely to be required.

Vitamin D₂

Viosterol (activated Ergosterol) is a convenient form of vitamin D₂ for incorporation into cosmetic preparations. It is generally available as a yellow oil containing 1 to 2 million units of vitamin D₂ per gram. Viosterol in oil is insoluble in water, but is soluble in fats and oils. It can be solubilized in aqueous solutions in the same manner as vitamin A palmitate. Vitamin D₂ is relatively stable to heat and to oxidation in oil solution, but is quite unstable in the presence of mineral salts. Since mineral salts are normally not present in cosmetic formulations, no precautions or stabilizing ingredients are required in the incorporation of vitamin D₂.

Vitamin E

Vitamin E activity is imparted by either the acetate ester of vitamin E or by the alcohol form. The ester, a stable and active form of vitamin E, is a yellow, viscous oil. It is insoluble in water, but is soluble in alcohol, fats and oils. It can be solubilized in aqueous solutions in the same manner as vitamin A palmitate. It is unstable in the presence of alkalies and is affected by light.

Incorporation of the Water-Soluble Vitamins

The water-soluble vitamins may be incorporated directly into the aqueous phase of the cosmetic preparation or, in the absence of an aqueous phase, intimately dispersed in the oil phase.

Biotin

Biotin is a white, crystalline compound, slightly soluble in water and in alcohol, but insoluble in fats and oils. It is stable to air and heat in acid and alkaline solutions at pH 4 to 8. It is inactivated by oxidizing agents. Biotin is readily soluble in dilute solutions of alkali hydroxides and can be conveniently incorporated into cosmetic formulations in this form.

Panthenol

Panthenol is available in two forms, namely, the dextrorotary isomer, d-panthenol, or the racemic form, dl-panthenol. The physiological activity of the racemic form is one-half that of the dextrorotary isomer. d-Panthenol is a colorless, viscous liquid, while

dl-panthenol is a white crystalline powder. d- and dl-Panthenol are both very soluble in water and in alcohol, but are insoluble in fats and oils. Aqueous solutions of d- and dl-panthenol are most stable in the pH range of 4 to 7, the optimum pH being approximately 6. Hydrolysis occurs at an increasing rate as the pH varies from the optimum pH as reported by Rubin.⁷⁰

Pyridoxine Hydrochloride

Pyridoxine hydrochloride is a white crystalline compound, soluble in water and in alcohol, but insoluble in fats and oils. Aqueous solutions are stable to air and heat in acid solution and in alkaline solutions up to a pH of about 8.4. Solutions are affected by light and discolor slightly.

Multivitamin Topical Products

Our treatment of the vitamins in the preceding has been essentially entity by entity. This does not imply the desirability of topical products containing only a single vitamin. On the contrary, just as with oral and parenteral products, it is recognized that multivitamin formulations are indicated. There are topical products in wide distribution that employ the advantages of the synergistic or complementary effects of several vitamins both oil and water soluble.

The growing interest in these type formulae augurs well for their future in many areas of use and treatment.

Overages

The slight losses of vitamin content of cosmetic preparations incurred during manufacture and storage can be compensated by including a suitable overage of the vitamin. In the case of the stable compounds, such as vitamin D₂, vitamin E (dl- α -tocopheryl acetate), biotin and pyridoxine hydrochloride, a 1 to 10% overage is usually included to compensate for loss during handling and to assay variation. For panthenol, the required overage is dependent upon the pH of the product, with 30% overage being sufficient at pH 4 and 10% at pH 6. In the case of vitamin A palmitate, a 25% overage is usually sufficient for most products. The amount of overage, in all cases, must be carefully determined on the basis of proper tests on the individual formulations.

Cosmetic Vitamin Formulations—Typical Formulae

As mentioned in the forepart of this presentation, cosmetic chemists should not experience difficulty in preparing creams, lotions, pomades or other cosmetic products with an adequate and stable multivitamin component. Generally, products now in distribution by a given producer may serve as a carrier of vitamin entities. Formulae of vitamin A and vitamins A and D dermatologic ointments have been suggested by Lesser.⁷¹ Since such formulae represent the dispersing or emulsification of lipid materials, vitamin E (and other oil-soluble entities) may be included. Vitamin A and D ointment formulae are also discussed in an official compendium.⁷²

Hydrophilic ointment U.S.P.⁷³ may be modified quite extensively and thus serve as the basis for a multivitamin cream having characteristics required for special cosmetic and therapeutic uses.

Summary

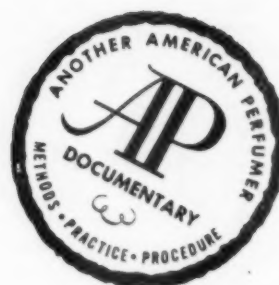
1. Adequate vitamin intake is necessary to maintain nutrition and integrity of the skin.

2. Vitamins are a nutrient to the skin and appear to also have a beneficial local pharmacodynamic effect.
3. Both the oil-soluble and the water-soluble vitamins are contained in presently marketed topical products.
4. Cosmetic vitamin formulations are relatively easy to prepare.
5. Techniques for formulation and suggestions for typical formulae have been outlined.
6. Overages are suggested to maintain label claim and cover small losses that may be incurred during manufacture.
7. Continued and expanded clinical research by the cosmetic manufacturer is necessary for the industry's future growth.

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The Use of Estrogens and Other Hormones



. . . A Series Of Questions & Answers

Various questions have been raised by different people either in print or in oral presentations regarding the usefulness of estrogenic hormones in cosmetic creams and lotions. Skeptics have used various ways of expressing themselves and one sometimes wonders whether the speakers have all the facts on the subject or whether they are speaking extemporaneously from something they had heard or read at one time or other.

To this extent, your editorial director addressed a number of questions which have been raised over the years to Dr. Max A. Goldzieher, one of the pioneers in determining the value of estrogenic hormone creams to the female human skin.

Dr. Goldzieher was very brief in his answers but this very brevity is quite to the point. We feel privileged to present the opinions of such an expert, particularly in the light of utterances of speakers appearing before the Society of Cosmetic Chemists in recent years and also publications appearing in the domestic lay and professional press of this country and Europe.

Q. It has been said that if postmenopausal women used an estrogenic cosmetic containing 10,000 I. U. per ounce, that there is a tendency for growth of an epithelial tissue over the uterus and that spotting of this tissue can result. What can you tell us about this?

A. *Not true.*

Q. Some people in the medical field have grave doubts that two ounces of cream a month containing 10,000 I.U. estrogen per ounce would do much good. Indeed, a publication by Berman showed that there was no advantage. What is your experience in this regard?

A. *Doubts are due to ignorance.*

Q. It has been stated that pigmentation of the skin may follow the application of an estrogenic cosmetic cream. Is this true?

A. *Not true.*

Q. Users of cosmetic creams have commented at times that they have noticed an increase in facial hair growth following the application of an estrogen-containing cosmetic. Is this possible? These are all postmenopausal women.

A. *Coincidence.*

Q. In 1945 at a meeting of the Society of Cosmetic Chemists, an endocrinologist suggested the use of progesterone along with estrogen in a cosmetic cream. He did not elaborate any further. What cosmetic effect could be expected from the addition of progesterone to the estrogen that is not obtainable from the estrogen alone?

A. *None.*

Q. At a later meeting of the Society of Cosmetic Chemists, you made the statement that an "ugly skin yields" to skin applications of thyroid. Why isn't thyroid used more in dermatological ointments if this is so?

A. *Thyroid should be used only orally. There is no incidence that it is effective topically.*

Q. Do you think diethylstilbestrol is as effective and more safe than estrone in cosmetic creams and lotions?

A. *No difference.*

Q. With the introduction of placenta extracts in which 1 cc. of extract represents at least the active ingredients of 1 gram and as much as 3 grams of placenta, is it possible that these extracts are more effective because of their composition of estrogens, progesterones, and other valuable factors over estrogens alone?

A. *Unlikely.*

Q. What do you think of the compounds that have been recently patented (U. S. Patent No. 2,845,381) belonging to the androstan series but having no sexual activity as being superior in their skin stimulating and cosmetic effect than the estrogens? One of the specific compounds mentioned is Δ^5 -androst-3 β -ol?

A. *Have no personal experience.*

Q. Lehman recently reported no histopathological changes in skin of virgin female albino rabbits following the daily application of 250, 500, 1,000 and 4,000 I. U. estrone five days a week for 90 days. How do you account for this in the light of your own experiments followed with biopsies?

A. *I never worked on rabbits' skin. The rabbit may be unsuitable for such experiments. My work was done on humans. Repeated interruptions (2 days weekly) cannot help but confuse the issue. Applications should be continuous for 3 weeks to show results.*

Q. Lehman further used larger doses, 1,000 and 5,000 I. U. estrone daily for 5 days of each week for 18 months. He reported only a "slight increase in epidermal thickness" and some reduction of the number of hair follicles. Why do these results vary so much from your own published findings?

A. *The changes observed in women are not limited to the epidermis. They include also regeneration of the elastic fibers, as corroborated by Chieffi with the help of an independent technique.*



A CONTRIBUTION TO THE STUDY OF SOME ORGAN EXTRACTS

All the great medical discoveries were not made in the U.S.A. To this end to get a better view of the use of organ extracts, the following article presents the observations of Dr. Jean Cotte, which were presented recently at Bonn, Germany before the International Symposium Gesellschaft Deutscher, Kosmetik Chemiker.

DR. JEAN M. COTTE

The Filatov theory of tissue therapy is essentially based on the fact that animal or vegetable cells, when submitted to unfavorable conditions of living, secrete stimulating substances which have been called *biostimulins* and can be considered as the expression of a struggle for life on the part of the cell. What characterises Filatov's theory is universality:—*universality of origin*: only unfavorable conditions of living can produce such substances;—*universality of action*: from the start the Russian clinicians applied this therapy to extremely varied fields.

Nevertheless, the nature of the tissue is not altogether

specific; in most cases it is the placenta that has been used. From human placenta were prepared either various extracts or grafts whose action results in an increase of cell metabolism, a stimulation of various physiological functions, and a rise in regenerating processes that were sanctioned by a host of therapeutic indications. We mainly explored the field of dermatology under the direction of Gate, a Professor in a dermatological clinic at Lyons University. What struck us most at the time was the spectacular action as a healing agent (1). In some cases, the healing process was such that it became compulsory to "nitrate" the regenerating wound so as to prevent a bad scar from setting in.

Numerous hypotheses have been put forward by vari-

* LYON, FRANCE

ous authors concerning the nature of *active principles* in Filatov extracts. We shall point out only what we have been able to ascertain for ourselves on the matter.

Ever since we began our clinical study, we had been struck by the fact that, with patients treated, Thorn's test rapidly proved positive, which means that tissue therapy acted as a stimulant for the formation of ACTH or the liberation of corticoids (2). Then, working upon this hypothesis, we tried to show up a few cortex stimulating substances in the placenta. This proved to be a real problem. Finally isolated a comparatively pure preparation which has an ACTH activity comparable to the best trade products (3). Some of the anti-inflammatory properties of placental ointment and powders are related to this action.

Recently, Vairel and Choay succeeded in isolating a substance which rates high in the bio-stimulating qualities that are recognized in tissue extracts (4). Lastly, Ratsimamanga, taking up Sato's works, isolated an anti-toxic principle from the liver (5). This, however, is not specific to the said organ since it has proved possible to draw it from the skin, the spleen, the brain, etc. . . . The author points out that activity of such a principle is not due to one body, but to the synergic action of a whole group of substances some of which have already been detected and belong to the amino-acid group. These conclusions are, it seems, particularly important, and we shall come back to them later on.

It is most obvious that the interesting results obtained through biological therapies in dermatology (6) immediately suggested cosmetological applications, and this is the aspect that we have been considering for the last 2 years (7): On the one hand, extracts of the Filatov kind, that is to say aqueous extracts containing hydro-soluble and thermostable substances; and total lyophilised extracts containing mainly enzymes and treph-ones.

Lastly, we used three kinds of organs: human placenta, bovine embryos, and bovine conjunctive tissue. The clinical experiments on some of these products is still going on.

Preparation of Extracts

a) *Extract making and choice of organs.* The organs are taken out according to a strict cold chain and frozen

Average Composition of Organ Extracts

Ex-tract Day	Sodium m.Eg. % gr. %	Po-tassium m.Eg. % gr. %	Chlo-ride m.Eg. % gr. %	Phos-phor-ous mgr. %	N Total gr. %
Placenta					
Aqueous Extract 11-14	40-50	15-20	42-56		1.2-1.4
50%	0,920-1,150	0,585-0,780	1,5-2		
Glycerol-Glycolic Extract	20-30	5-10	22,5-28	75-80	1.2-1.4
	0,460-0,690	0,195-0,390	0,8-1		
Total Extract	70-80	18-23	85-100	200-250	6,5-7,02
	1,610-1,840	0,702-0,897	3-3,5		
Embryonic					
Aqueous Extract 14-16	25-34	20-25	25,35		
50%	0,575-0,782	0,780-0,975	0,9-1,25		
Total Extract	55-65	25-30	52-65	225-275	1-1,3
	1,265-1,495	0,975-1,170	1,85-2,3		3,4-3,8
Conjunctive Tissue					
Aqueous Extract 48-52	45-55	20-25	42-57		6,2-6,8
50%	1,035-1,265	0,780-0,975	1,5-2		
Total Extract	80-90	52,5-57	71-85	400-450	5,8-6,2
	1,840-2,07	2,047-2,223	2,5-3		

at once. When an embryo and a conjunctive tissue of bovine origin are required, the animal is killed in the presence of a specialised veterinary surgeon who takes

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out the various organs to be used. The embryo tissue utilised to make the extract is composed of the liver, the adrenals, the lungs, the spleen, the heart, the thymus, the brain, the cerebellum of comparatively young embryos: embryos weighing more than 300 gr. are all rejected. The conjunctive tissue is composed of dermic and hypodermic tissues taken from embryos of older bovines.

b) *Aqueous extracts of the Filatov kind*: such extracts are prepared according to now well set techniques. They are sterilised. The placental tissue is given a special treatment at the start in order to rid it of its blood so as to keep only the placental and to extract only the tissue substances.

c) *Total lyophilised extracts*: they are prepared after crushing operation which should be performed immediately after the organ has been taken out. Crushing is effected through special process which consists of a series of freezing and thawing operations one after the other intended to burst the cells. The final extract undergoes several purifying operations, after which it is lyophilised because the active principles are so unstable. Such extracts are preserved under inert gas.

d) *Glycero-glycolic extracts*: the human placenta is used to prepare a glycero-glycolic extract meant to give a richer extract. This was obtained from chromatographic study on paper of amino acids.

Physico-Chemical Study

Table 1 gives the average composition of various organ extracts. We shall insist on the fact that we particularly dwell on the mineral composition, that is to say on the ions, sodium and potassium, representing the cell level which we reach through the various extraction processes. The sodium ion is essentially an extra-cellular ion, while the potassium ion comes mainly from the cell. The lower the ratio between sodium ion and potassium ion, the more complete the extraction process, and the various figures come to unquestionably prove that we reach the cell itself. Whenever we altered the extraction process, we always found, as a matter of fact, that the potassium figures fell heavily, the ratio between sodium and potassium then rising to values 5 to 6 times higher.

Lastly, we made a thorough survey of the nitrogen in the various kinds of extracts. This question appeared to us as a very important one since, from the beginning of therapeutic experiments on placental extracts, the ultra filtration of an extract through a collodion candle allowed a more active fraction to be isolated which did not pass through the membrane (8). We then set a protein limit for therapeutic extracts.

Extracts to be used in cosmetics can contain larger quantities of proteic nitrogen; the preparation technique as well as the extraction process were modified accordingly. The various procedures we go through show the importance of these two points in the production of particularly active extracts.

As a matter of fact, the importance of the nitrogen foundation, discovered by ourselves in the course of therapeutic experiment (8), has just been again stressed and confirmed by Ratsimamanga's works (5). *The nitrogen foundation can really be considered as the vehicle for active principles in this kind of preparation.* This conclusion is the fundamental element of the whole of our experiments.

Thanks to the paper chromatographic separation of amino acids, we were able, on the one hand, to determine the best conditions for the preparation of various extracts, and, on the other hand, make out real identity cards of these products. This technique was used in order to explore the nitrogen constituent of organ ex-

tracts more thoroughly and with more precision.

The nitrogen of various organ extracts is mainly represented by protein nitrogen, the quantity being much lower for Filatov extracts.

After hydrolysis, about fifteen amino acids can be detected, viz.: aspartic acid, glutamic acid, serine, glycocoll, threonine, alanine, tyrosine, lysine, histidine, arginine, oxyproline, valine, phenylalanine, leucine-isoleucine, proline, and more seldom, traces of cystine.

If chromatographic isolation takes place before hydrolysis, the number of spots is generally fewer, especially in the case of total lyophilised extracts which are rich in protein nitrogen. Chromatography used before and after hydrolysis therefore allows each kind of extract to be characterised quite precisely, and above all the real composition of product presented to be determined chemically.

It is obvious that total lyophilised extracts contain comparatively important properties of *enzymes*. We especially looked for phosphatases, alkaline and acid, oxydases and peroxydases, which we titrated. The titration of acid phosphatases is particularly high. The enzymatic activity of aqueous extracts of the Filatov kind is very low and some times nil, which is obvious, considering the way they are prepared.

As to the various hypotheses on the nature of active principles, we shall recall that we were able to isolate a substance with a *cortex stimulating activity* (3). But the action of this kind of product is not strictly cortisone-like.

Experiments carried out in Tübingen, under the direction of Butenandt, showed the presence of *nucleic acids* in placenta extracts (8). This is not surprising but it shows that the extraction processes used liberate the most intimate cell substances.

Lastly, dialysis as well as the ultra-filtration showed that 55 to 60% of components pass through the membranes and that the fraction that does not go through is more active in the healing of wounds (8).

Biological Study

We studied the action of various extracts on vegetable growth (lentils). At fairly high concentrations utilised, —up to 1%—we noted a distinctly retarding action on the growth of stems. Increased dilution does not show a very distinct stimulating action, but these experiments are yet to be completed.

The addition of placenta extracts to *culture media* of some *lactobacilli* very distinctly increase the production of lactic acid. Meyer and his collaborators (9) repeated with particularly exacting micro-organisms and were able to establish direct relation between bacterial metabolism and quantity of biostimuline in certain organ extracts.

Beside the cortex stimulating action previously pointed out, we only noted a constant increase of the blood alkaline phosphatase activity. This element appeared important, considering the relation existing between the phosphatase activity and the synthesis of fibrous proteins (Danielli).

We shall lastly point out the return to the normal figure in the ratio between blood clotting rate and the number of red corpuscles with old people injected with total lyophilised embryo extracts. Said ratio, as shown by BINET, becomes higher with old people: this therapy is therefore particularly active in senescent conditions. Besides, considering the importance of sulphur containing amino acids in skin metabolism, this fact should be stressed.

Cosmetic Indications

The results obtained in therapy and a number of observations made in the course of a fairly wide range of experiments have allowed us to state the cosmetic indications for organ extracts thus prepared.

There are now a host of works concerned with tissue therapy by external methods. Placenta creams and powders have a trophic healing action which is easy to set off, and we, ourselves, in the course of our experiments, using techniques proposed by LeComte du Nouy (weighing the tracing of a wound surface), were able to measure the healing speed of pathological or experimental wounds (8). This trophic skin action is only the dermatological projection of more general effects in varied fields, but wherein always found the metabolic stimulation of regeneration processes: such as results obtained in geriatrics and pediatrics shown up by humoral alterations or weight graphs, or again the healing action evident in gastric ulcers of placenta grafts, etc.

Cosmetic practice could consequently find in tissue extract just a particularly privileged choice of raw material, on condition, of course, that manufacturing standards be complied with so as to offer products in all points similar to those used in therapy.

Said therapy now calls upon other biological products, such as embryo extracts used in France by 2 particularly qualified specialists, Pasteur Valéry Radot and Leon Binet. These two physicians set out on a therapeutic study of old people, and noted an improvement in their condition not only through mere clinical observation, but also by means of precise laboratory tests. Binet, talking precisely about observed humoral alterations, concludes his official report in the following way: "such facts seem to prove the favorable, powerful effect of embryo therapy applied to senescent men. We have no hesitation concluding that the human body, when advanced in years, benefits by the bringing into it, embryo extract prepared so as to maintain fully active principles and physiological qualities."

Cosmetic indications most naturally come out of results observed in therapy (10). Organ extracts with a general effect on all metabolism will find an application in all cases of normal or premature senescence and all unesthetic manifestations of certain cases of unbalance. Each kind of organ has its own polarity:

Placenta extracts are particularly interesting in breast modelling. Their firming effect shows up after a series of 15 to 20 applications (preferably glyceroglycolic extract). A wide range of experiments which are being carried out now determine this effect more completely.

Placenta extracts are also being used in face massaging or on tissue to soften it. (Filatov aqueous extracts or total lyophilised extracts).

Embryo extracts are used in all unesthetic skin manifestations of senescence.

Conjunctive tissue extracts due to their composition, find a choice application in the prevention and treatment of wrinkles, their surface mechanical action being indeed non-negligible and thus completing a deeper action. The Filatov aqueous extract of conjunctive tissue is more especially used in massages against cellulitis. Therapeutic experiments are being carried out in specialised departments in order to show how this original product works.

Under What Form and How Used

The organ extracts we used (10) correspond to the three kinds of organs already mentioned, in 2 different forms:

aqueous extracts representing 50% of organs;
total lyophilised extracts corresponding to a determined weight of organs.

Moreover, the placenta allows a special glyceroglycolic extract to be prepared, rating 50% in placenta.

Total lyophilised extracts have the advantage of a very high active power under comparatively small weight. They keep well in sealed bottles which makes them easy to stock, preserve and use.

Said extracts can be utilised either alone, or dispersed in various adequate cosmetic preparations (various creams and milk).

Aqueous extracts of the Filatov kind are applied directly on the skin after cleansing it thoroughly with a lukewarm cleansing agent. This causes a certain amount of vaso-dilatation which favors further absorption.

Total lyophilised extracts are used under the same conditions after reconstitution corresponding to the weight of organs with appropriate fluid. The solvent can be either buffered isotonic water, or one part water and two parts glycerol, better still, a 30% emulsion of interesterified oil (11) which greatly facilitates the skin absorption.

The glyceroglycolic placenta extract is applied undiluted in light massages of the breast. The series of applications are normally 15 to 20, between the menstrual periods.

Cosmetic Preparations

Said organ extracts can make up the active part of cosmetic preparations, of the o/w emulsion kind.

The glyceroglycolic placenta extract is used as it is in proportions of 30 to 30%. It seems preferable to use it every time it is possible to do so since it keeps perfectly. The Filatov aqueous extracts should be added with 25 to 30% glycerol before dispersion. They are then utilised at similar concentrations.

Total lyophilised extracts are dissolved in a mixture constituted by 2 parts glycerol and one part water for 3 cc of solvent with what corresponds to 2 gr. of organs. Solutions thus prepared remain fully active and are then utilised in proportion of 10 to 50% in the various cosmetic preparations. With lyophilised extracts, one should see that all traces of heavy metals are eliminated (anti-enzymatic action.)

Various cosmetic products with organ extracts as foundations complete the treatment itself (day cream or night cream), by permanently ensuring the highly bracing action of the cell or tissue substances.

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QUESTIONS & ANSWERS

1335 REJUVENATION CREAMS

Q. Please send information about products being incorporated into co-called "rejuvenation" cosmetic creams that are now being widely advertised. The products we have in mind are essential polyunsaturates, bio-energizers, placenta extracts, vitamins A, D, E and B₁₂. Could you supply us with sources of supply and literature references? We are interested in preparing such a cream and would like to have you supply us with basic formula. Q. A. W., Mass.

A. Information on the products you mention can be found in German and French trade journals, such as COSMETOLOGIE from Editions Varia, 28 rue Serpente, Paris VIe, France, and FETTE, SEIFEN ANSTRICHMITTEL from Industrieverlag von Hernhausen K. G., Hamburg 11, Germany. Unfortunately, we do not know what you mean by "bio-energizers." However, the other raw materials you list can be obtained from the following suppliers. Essential Polyunsaturates: Van Dyk & Co., Main and William Streets, Belleville, New Jersey; Placenta Extract: Merz & Co., Eckenheimer Landstrasse 100-104, Frankfurt a/M., Germany; Dr. Kurt Richter GmbH., Benningsenstrasse 25, Berlin, Germany; Vitamins A, D, E and B₁₂: Merck and Company, Rahway, New Jersey. We are enclosing a formula from Sagarin's book, COSMETICS: SCIENCE AND TECHNOLOGY, page 120. This book is available from the book department of the AMERICAN PERFUMER.

Formula 24*		
(Emollient Cream, Nonionic W/O Type)		
	Light Mineral Oil	25.0 %
	Microcrystalline Wax, M.P. 79.5°C.	5.0 %
A.	Amerchol L-101*	10.0 %
	Lanolin	10.0 %
	Propyl Paraben	0.15%
	Methyl Paraben	0.15%
B.	Water	49.4 %
	Perfume	0.3 %

*"Emollient Creams and Lotions," by Gabriel Barnett, in COSMETICS: SCIENCE AND TECHNOLOGY, *American Cholesterol Products, Edison, N. J.

1336 TIOGLICOLI ACID

Q. We wish to purchase a book describing the process for obtaining tioglicoli acid. We would also like to know of a supplier of Deprovivynoll. R. C., Brazil.

A. We presume you mean thioglycolic acid and to our knowledge there is no book giving the methods of its manufacture. The classical laboratory methods are the ones that have been used. Some start with monochloroacetic acid and others start with thiohydantoin. We suggest you refer to a textbook on organic chemistry for the exact procedure. Unfortunately, we do not know what you mean when you ask about deprovivynoll. We have never heard of this compound. If you mean polyvinylpyrrolidone, then we can tell you that this can be purchased from General Aniline and Film Corp., 230 Park Avenue, New York.

1337 DAMASCENIN

Q. We would appreciate receiving the name and address of the manufacturer of Damascenin (nigelline or methyl 2-methylamine 3-methoxybenzoate). C. H. A., Puerto Rico.

A. We regret we do not know a supplier of Damascenin and are sorry we cannot help you.

1338 CUTICLE REMOVER

Q. There is a cuticle remover on the market under the name of Blue Cross Cuticle Remover. Will you kindly give us the name and address of the manufacturer of this product? M. C. S., Illinois.

A. As far as we know Vi-Jon Laboratories, Inc., 6300 Etzel Avenue, St. Louis 14, Missouri, are still manufacturing this cuticle remover.

From time to time suggestions have been and will be made in this magazine with respect to processes, devices, materials, appliances, equipment and the like. It is not practicable for the writer and editors to have a patent search or examination made in connection with each such suggestion. Our readers are, therefore, requested and indeed urged to determine for themselves whether any patent or other right will be violated before acting on any such suggestion.

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TECHNICAL

ABSTRACTS*

The Editors are pleased to present the following abstracts presented in London in April.

FILTRATION FUNDAMENTALS

D. M. Wyllie

The generally known basic filtration equations are discussed, giving the factors governing the flow of liquids through porous media. Simple filter media and the use of filter aids are dealt with, and the influence of pore size and porosity is explained. These considerations, together with surface area and adsorption effects, are correlated with problems occurring in the cosmetic and pharmaceutical field, such problems being split into the separation of a solid and a liquid phase from a required liquid phase.

The theoretical principles of filtration developed should enable suitable processes to be chosen for particular purposes.

THE PRESENT STATE OF THE COSMETIC INDUSTRY

W. S. Bullough

The author stresses the lop-sided development of the Cosmetic Industry, which has concentrated on the application of scientific methods to the manufacture of its products, but has neglected their application to the study of the metabolic processes of the skin. He emphasizes the Industry's need to adopt an ethical approach to its activities which are really a branch of preventative medicine, and to abandon its addiction to secret arts.

RECENT ADVANCES IN THE BIOLOGY OF SKIN

F. J. Ebling

The formation and turnover of epidermal cells and the latest work on the effect of nutrition, hormones and other factors on the epidermis is described. The trans-

port of water and topically applied substances through the epidermis is also dealt with. The lecture concludes with a discussion of modern concepts of the changes which occur in the skin during ageing and of factors which affect the growth of hair.

COSMETICS, ALLERGY AND SKIN

J. G. Feinberg

The skin is a tissue of great interest to cosmetologist and allergist alike. Both, at times, must cope with its idiosyncrasies. Not infrequently their concern over the skin is mutual—such as when a cosmetic preparation produces an allergic reaction in a sensitive skin. The skin is not the only tissue to develop an allergy to cosmetics, but even at such times it may serve as a guide to the offending substances. The fundamental aspects of and experimental approach to these interrelated problems will be considered.

COSMETICS AS A FACTOR IN CIVILISATION

R. H. Marriott

The development of cosmetics is traced from their earliest probable use as protective measures against the elements through their use for drawing attention to the personality of the individual, to their wide use by diverse peoples in order to conform with an accepted standard of outward agreeableness, so making easier their living together in a modern civilisation.

The awareness by a person of his acceptance by the community is becoming recognized to be psychologically and somatically beneficial to him. Although it is right that cosmetics should be formulated so that they are physiologically correct, yet it would seem undesirable that they enter the field of medicine with the danger of re-establishing the practice of self-medication under a new guise.

*Presented at the British Congress of Cosmetic Science, London, April, 1959

ANALYTICAL METHODS IN ASSESSING THE VALUE OF PERFUMERY RAW MATERIALS

M. van den Dool

The methods of analysis of perfumery raw materials—essential oils or synthetic products—are discussed in relation to the particular problem involved. The spectrophotometric and chromatographic methods are reviewed and their application demonstrated. Attention will also be given to the combination of results of some classical methods.

ULTRA-VIOLET SPECTROPHOTOMETRIC PROCEDURES IN ESSENTIAL OIL EXAMINATION

J. B. Stenlake and W. D. Williams

The reducing action of sodium borohydride on α -unsaturated carbonyl compounds is used to determine such compounds in essential oils and commercial ionones by spectrophotometric means. The results on essential oils confirm earlier work in which Girard-T reagent was used.

SPECIFICATIONS FOR RAW MATERIALS AND FINISHED PRODUCTS

N. J. Van Abbe

Principles underlying the drafting of specifications of raw materials will be discussed. Finished product specifications should be employed in a works as manufacturing instructions and should give details of formula, processing technique, intermediate and final analytical control. It is desirable that arithmetical calculations in the production department should be avoided wherever possible.

TRENDS IN MECHANISATION IN LABORATORIES

R. Barrington Brock

Two fully automatic methods of analysis are roughly described and details are then given of the progress towards mechanisation with many of the normal types of test. Work on moisture testing, particle size measurement, viscosity measurement, and other physical tests is described and possible methods of mechanisation are discussed.

THE FUNCTION OF CONSUMER TESTING IN PRODUCT DEVELOPMENT AND MARKETING

L. H. Ovens

In the long run, it is the consumer who determines the level of success of new or modified products. At the laboratory stage of development great experience and skill can still err due, for instance, to testing in "ideal" conditions, or relying on opinions of people too closely connected with products. And, at the marketing stage, no amount of advertising will repeatedly sell an unacceptable product. Consumer product testing helps to illumine the unknown area between the laboratory and the shop counter, assisting the former and protecting against loss on the latter.

LABORATORY TESTS AS A BASIS FOR ACCURATE PRODUCT MARKET TESTING

Donald H. Powers

In the evaluation of cosmetic performance the use of panel tests frequently becomes a study in human behavior rather than product performance. By setting up accurate, reliable, reproducible tests for measuring prop-

erties of cosmetics it is possible to measure product differences in the laboratory. By panel and market testing cosmetics of known differences it is possible to assess reasons for consumer acceptance. Methods are described of measuring properties of shampoos, hair waving lotions, hand lotions, face powders, aerosols, antiperspirants and deodorants.

PRODUCT EVALUATION FROM THE RHEOLOGICAL ASPECT

L. S. Adler

This basic principles of assessment of the rheological properties of Newtonian liquids, plastic and pseudo-plastic materials are enumerated. Measurement of the two latter properties by the de Waele plastometer is described and its application to a particular system is demonstrated. Its use with toilet preparations is discussed.

PATCH TESTING METHODS

E. J. Moynahan

Patch testing can be used to diagnose the cause of any dermatological upset caused by cosmetics, and for the detection of potential irritants and sensitising agents. The use of animal experiments will be discussed and a model scheme will be shown for testing on human beings.

THE EFFECT OF RHEOLOGICAL PROPERTIES ON MIXING AND HEAT-TRANSFER OPERATIONS

E. S. Sellers and W. L. Wilkinson

For 'normal', i.e. Newtonian, liquids the analysis of accumulated practical and experimental data has enabled chemical engineers to produce general relationships to predict such things as power requirements in mixers and pumps, area requirements in heaters and coolers, and so on. Attempts are now being made to extend these general relationships to substances the rheological properties of which are definitely non-Newtonian. The effect of the rheological properties are discussed, with particular reference to the design of equipment for carrying out certain manufacturing operations.

HEAT TRANSFER IN COSMETIC MANUFACTURING PROCESSES

V. O. E. Bryant

During the last decade considerable attention has been focused upon the problem of heat transfer under wide and varied conditions. Much of this research has been brought about by the steep rise in the cost of solid fuel and the necessity thereby for greater fuel utilisation efficiency. The author seeks to re-consider the problems of heat transfer in cosmetic manufacturing plant in the light of this vast fund of new knowledge now being made available to industry generally.

CORROSION OF IRON AND ALUMINIUM

K. F. Lorking and J. E. O. Mayne

The current theories of the inhibition of corrosion of iron will be reviewed and it will be shown that they do not explain all the facts. A new theory will be put forward, which is more in accordance with the facts, and it will be shown how it leads to the development of methods of deciding whether a given solution is corrosive or inhibitive.

The present position with respect to the inhibition of the corrosion of aluminum will then be reviewed in a similar way.

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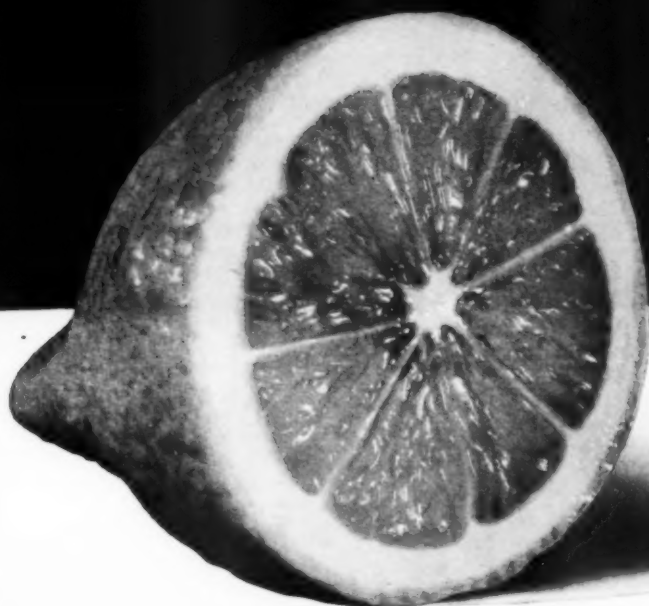


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- Charles Albert Smith Limited
- The University of Buffalo
- The Kamlet Laboratories
- Toni
- The Procter & Gamble Co.
- Prince Matchabelli, Inc.
- Lehn & Fink Products Corporation
- Vestal Incorporated
- Swift & Co.
- Pharma-Craft Corporation
- N.V. Chemische Fabriek
- R. H. Macy & Co. Inc.
- Atlas Powder Company, Canada, Ltd.
- University of Arkansas
- Hysan Products Co.
- Braun Chemical Co.
- Golden Peacock, Inc.
- Armour And Company
- E. I. DuPont
- Dept. of Health, Education, & Welfare
- State University Of Iowa
- The Hart Products Corp.
- Rockwell Products Co.
- The Dow Chemical Co.
- Aero-Chem Labs.
- Lawrence Richard Bruce Research Labs.
- West Laboratories, Inc.
- Royce Chemical Co.
- J. A. Tumbler Lab.
- Rohm & Haas Company
- Vytone Labs.
- Celanese Corporation Of America
- Foster D. Snell, Inc.
- Peck's Products Company
- Verona Aromatics
- Onyx Oil & Chemical Co.
- The Charles Marchands Co.
- Carroll Dunham Smith Pharmacal Co.
- Foremost Food & Chemical Co.
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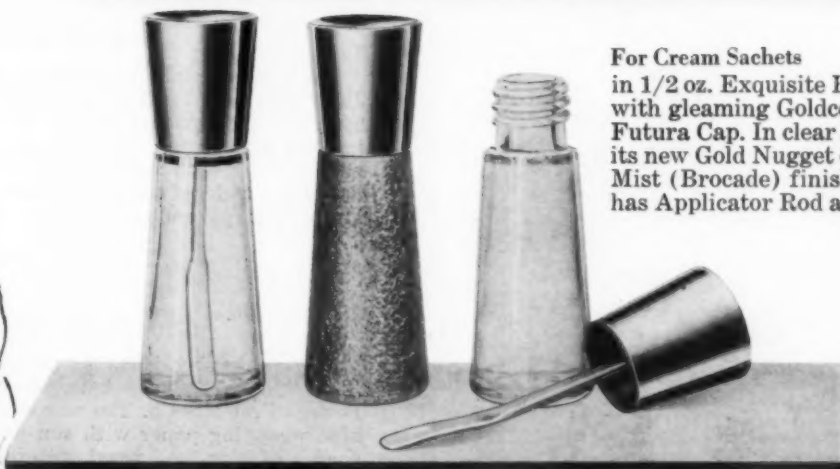
in Sachet Containers

A new flat oval 1½ oz. Jar, #1908—with or without Sifter Top and Goldcote Closure for sachet powder. And a companion 1/2 oz.,

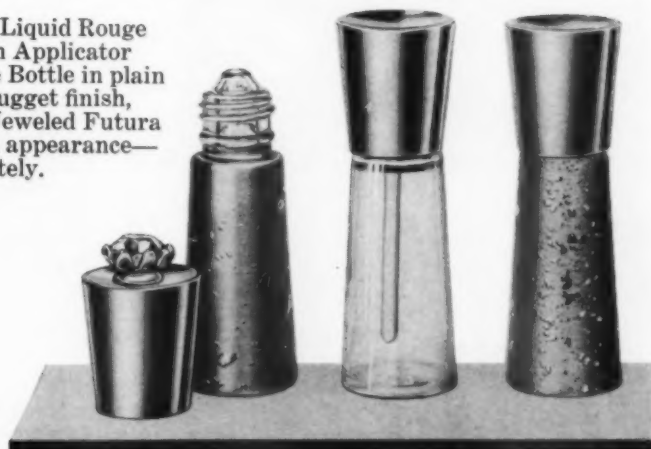
#R-33, Liquid sachet bottle with Touch-N-Flo dispenser unit—gold metal protector cap. (Patented)



For Cream Sachets in 1/2 oz. Exquisite Bottle with gleaming Goldcote Futura Cap. In clear glass or its new Gold Nugget or Gold Mist (Brocade) finish. Cap has Applicator Rod as shown.



A new 2 dram Liquid Rouge Container with Applicator Rod. Exquisite Bottle in plain or new Gold Nugget finish, with plain or Jeweled Futura Cap. Deluxe in appearance—priced moderately.



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MONICO—1

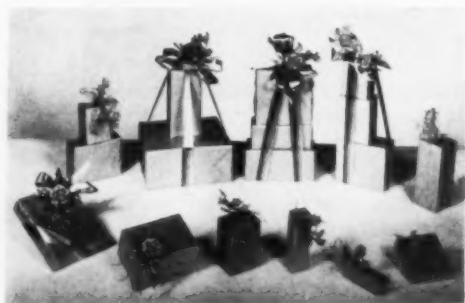
Three new product additions to their "Christmas in July" line have recently been introduced by Monico, Inc. They include a green Perfume Sachet enclosed in a gleaming red and white "book"; a luxuriously scented deluxe bath powder with feather puff, and a Cologne-Parfume Spray in a metered aerosol container. The three products are linked by a gold and red snowflake design.



1.

JOHN ROBERT POWERS—2

New packaging ideas for summer, called the "Happy Blues," have recently been introduced by John Robert Powers Products Co. The new designing combines silvery blue wrapping paper with sun gold cord, ribbons in rich shades of blue, and pearl-centered velvet flowers.



2.

REXALL—3

The Rexall Drug Company will soon be marketing three new toiletries in the "On Tap by Cara Nome" line. The new products, Brite Shampoo, Radiance Perfumed Hand Lotion, and Fast Clean, a deep facial cleanser, are all packaged in plastic-coated glass bottles by Owens-Illinois Glass Co. with low pressure aerosol caps designed for easy application. All are of the three-ounce size and are decorated in pastel shades.



3.

SIMONETTA—4

Made for travel convenience, Simonetta of Rome's new Incanto Cologne is presented in a new spray container holding 600 metered mist sprays. The golden metal leak-proof flacon is engraved with Simonetta's identifying Roman column motif and topped with an ebony cap. Scenes of ancient Rome by the famed 18th century artist Piranesi decorate all four sides of the white gift carton.



4.



5.



6.

LEHN & FINK—5

Etiquet Rolit, a roll-on deoderant in an unbreakable and spillproof plastic dispenser, has been newly packaged by Lehn and Fink Products Inc. The new compact carton is light aqua with bold red and white printing. Until June 12 the deoderant will be available in a "1 free with 11" offer, selling for 69¢.

BONNE BELL—6

Bonne Bell, who began promotion of the gallon jug of their "Ten-O-Six" facial cleanser as an advertising gimmick, reports that consumers willingly buy the economy size. As a result the large bottle has been newly decorated with a huge gold rosette bow and a gold-sprayed plastic funnel splashed with sequins.



7.

GUERLAIN—7

Guerlain announces a new lipstick case designed by one of France's most distinguished jewelers. The case is a slender ribbed silver-toned column etched with tiny sparkly dots and banded in burnished gold. It is easily refillable with any of Guerlain's nine lipstick shades, providing a whole wardrobe of colors in one holder. The new case retails for \$3.00 and refills cost \$1.00.

CIRO—8

This counter display by Parfums Ciro carries out a French tricolor motif. It will be used to display 12 little Parisian hatboxes each containing a 1¼-dram replica of one of Ciro's four famous import perfumes: Reflexions, Danger, New Horizons and Surrender. The miniatures are priced at \$1.50 each, available for "sampling" or for small gifts.



8.

News

and Events

SPEAKERS AT SYMPOSIUM



The speakers at the 5th Annual Open Symposium of The American Society of Perfumers pictured with two officers of the Society who presided at the meeting. (l. to r.) Harry A. Cuttler, Edward J. Shuster, A. L. VanAmeringen, Dr. Oliver Marton, Dr. F. Lohman, Edward C. Fearn, Dr. S. Jellinek and V. D. Johnston.

Perfumers Hold 5th Symposium Jellinek Honored

Upwards of three hundred members of the soap, perfume cosmetic and related industries gathered at the Essex House in New York on April 20, 1959 to attend the 5th Annual Open Symposium of The American Society of Perfumers. The timeliness of the Symposium theme, "Instrumentation and the Perfumers" was evidenced by the large attendance and by the interesting and lengthy discussion which followed the presentation of the papers.

The Symposium was divided into two sections with the first speakers discussing the present status of instrumental methods of analysis and their value to the in-

dustry. After a brief intermission, the remaining speakers, while attesting to the aid received from the instrumental methods, confirmed the role of the perfumer as the final arbiter in the odor analysis and evaluation of perfume materials.

During the proceedings, an honorary membership in The American Society of Perfumers was bestowed upon Dr. P. Jellinek of Polak's Frutal Works in Holland in recognition of his many contributions to the field of perfumery. The Certificate of Honorary Membership was presented to Dr. Jellinek by Dr. Oliver Marton, President of the Society.

Grants-In-Aid By Hercules Powder

Approximately \$100,000 in unrestricted grants-in-aid is being distributed by Hercules Powder Company among nearly 30 colleges and universities.

This continues Hercules' long-standing program of financial aid to institutions of higher education. The unrestricted grants-in-aid program gives complete freedom in the use of these funds to the heads of departments of chemistry, chemical engineering, physics, mechanical engineering, and others in the participating schools.

"We believe it is in the nation's best interest that everything possible be done to strengthen the American educational system. We also believe that educators themselves know best what is needed to achieve this desired goal," said Albert E. Forster, president and board chairman of Hercules.

Seven of the grants were made to chemistry departments, eight to chemical engineering, five to mechanical engineering, and the remainder to a miscellaneous group including engineering physics and business administration.

Among the colleges and universities receiving the grants-in-aid this year are: California Institute of Technology, College of William and Mary, Cornell University, Georgia Institute of Technology, Harvard University, Illinois Institute of Technology, Johns Hopkins University, Kansas State, Lehigh University, Massachusetts Institute of Technology, McGill University (Canada), Mississippi State, North Carolina State, Ohio State University, Pennsylvania State University, Polytechnic Institute of Brooklyn, Princeton University, Rensselaer Polytechnic Institute, Rutgers University, Swarthmore College, Stevens Institute of Technology, University of Delaware, University of Illinois, University of Michigan, University of Pennsylvania, University of Virginia.

Recipients are selected from year to year on a cyclic basis in order to distribute funds available to the greatest number of schools and departments.

The selection of schools has been on a very broad basis, determined by factors such as the academic standing of the school and of its Science and Engineering Departments, the number of alumni from the particular school employed by Hercules, its proximity to Hercules plants and industrial locations, and the acuteness of the need.

FTC Dismisses Roux Case

The FTC has entered an order dismissing its complaint against Roux, which had been charged with unreasonable restraining trade and enforcing arbitrary classifications on its wholesale customers, to the detriment of their freedom to compete. The Commission held that a restriction as to whom the purchaser may resell, except where unlawful resale price maintenance is involved, is not illegal of and by itself, in the absence of a showing that such restriction has substantially lessened competition.

Motivation Research and Good Packaging Stressed at Canadian Meeting

Looking toward the wants and interests of Canadian women, two talks before the Toilet Goods Manufacturing Association, Toronto, stressed the value of motivation research for determining the needs of the feminine market and the importance of good packaging for capturing that market.

C. J. Laurin, director of the magazine division of Maclean-Hunter Publishing Co., presented the findings of a motivational research inquiry which brought to light the new freedoms and opportunities and the widened curiosities of modern Canadian women. In publications aimed at them, he said, these women are looking for stimulation, guidance, and a recognition of their new roles in Canadian life.

Clair Stewart, art director of Ralph Clark Stone Ltd., commenting that packaging is probably the most important instrument in merchandising a product, emphasized the importance of the art of typography in package design. A good package, he said, must be attractive, consistent, dominating, economical, and must easily identify the product it contains.

Canco Official Sees Trend To Use Of Aluminum

The possibility that aluminum cans may be seriously competitive with tin plate cans within the next ten years has been indicated by F. B. Newcomb, an official of American Can Company's Canco division.

Newcomb, vice president in charge of the division's commercial development, told the 28th National Packaging Conference, in Chicago, April 14, that his company was "willing to commit increasingly greater research funds on the gamble that the price of aluminum will be reduced enough to make aluminum cans competitive with tin plate cans."

The Canco official said the can-making industry is eager to have aluminum as a second can-making metal, but observed that the economics of aluminum and problems arising from the use of a light-gauge material are major hurdles to be overcome. He said his company's studies confirmed the finding of an industry sur-



A place for toiletries in the kitchen was the theme recently developed at the Design Center, New York City. In cooperation with Nevamar who designed the kitchen, it is now possible for the housewife to open the refrigerator door, or some other convenient door, and she will have her hand lotion. Houbigant, Inc. participated with their *Quelques Fleurs* toilet water.

vey in mid-1958 which pointed to a 20 per cent share of the metal container market for aluminum within the next decade.

D&O To Present \$1,000 Scholarship Award

To encourage deserving and outstanding students to take undergraduate work leading to a Bachelor's Degree in Food Technology, Food Engineering or Food Science, D&O is presenting this year a \$1,000 scholarship under the auspices of the Institute of Food Technology.

An applicant to qualify must be a

citizen of the United States or Canada and must have fully completed, prior to the effective date of the award, two full years of college work at a recognized educational institution in the U.S. or Canada. Candidates are judged on overall ability including scholarship, personality, extra curriculum activities, social adjustment, character, etc. by a special committee set up by the Institute of Food Technology.

The actual presentation of the plaque that accompanies this award will be made at a meeting of the Northeast Section of the Institute of Food Technologists in Boston at a later date.

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New Morningstar-Paisley plant in Clifton, N. J., has gone onstream with the production of polyvinyl acetate emulsions. Output of the new plant combined with a 50% increase in the PVAc production at the company's Chicago facility has doubled M-P's total capacity.

Morningstar-Paisley Doubles Output Of Polyvinyl Acetate Emulsions

Production of polyvinyl acetate emulsions has begun at the recently completed Morningstar-Paisley plant in Clifton, N. J., according to an announcement by Murray Stempel, executive vice president. In the same announcement it was also revealed that the company's Chicago plant has increased its output of these emulsions by 50%. As a result, total Morningstar production of these materials has been doubled. Mr. Stempel states that the additional facilities were made necessary by the increasing use of polyvinyl acetate emulsions in the adhesive and

coatings compounded by Morningstar.

The Clifton facility will give Eastern users faster delivery and closer contact with Morningstar's technical service and production team, according to Mr. Stempel. Standardization of products made in Clifton and Chicago has been attained through duplicating equipment in both plants.

Malmstrom Receives Safety Citation

The Malmstrom Chemical Corp. of Newark, N. J. has been awarded a Citation of Merit in the New Jersey annual safety contest for working throughout the year 1958 without suffering a disabling injury. The award was presented to the company representatives in Newark

at a dinner last month co-sponsored by the New Jersey State Department of Labor and the State Industrial Safety Committee.

Janovsky Addresses Convention

The National Fruit & Syrup Manufacturers Association, Inc., held its biggest convention, its forty-second, on April 17 and 18th at the Savoy Hilton Hotel in New York City. Victor E. Savin, director of restaurants for H. L. Green Co., Inc., spoke on the subject of the soda fountain and its importance to the fruit and syrup industry.

Harold L. Janovsky, Chief Flavor Chemist of Fritzsche Brothers, Inc., de-

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livered an illuminating address on practical flavor technology. Included in the program was an industry round table discussion, which concerned itself with new laws affecting the industry.

California Association Sponsors Banquet Honoring Max Factor

Plans for an elaborate banquet to honor the fiftieth anniversary of Max Factor & Co. were announced at the April meeting of the California Cosmetic Association.

An association committee of twenty-two members headed by Arnold L. Lewis as general chairman has completed arrangements for the event to take place at the Beverly Hilton Hotel, Beverly Hills, Friday evening, June 26th. In announcing details of the celebration, Mr. Lewis stated that three generations of the Factor family, now active in the operation of the firm, will be present at the banquet to witness a special commemorative presentation which will be part of the evening's program.

In concluding his announcement, Mr. Lewis commented that while the association was sponsoring the banquet, it was most desired that the event be considered a tribute on the part of the entire cosmetic industry.

Record First Quarter Sales at Heyden Newport

First quarter sales of Heyden Newport Chemical Corp. rose 25% above those for the same period of 1958 to set a high for any quarter in the corporation's history. S. Askin, president, announced in April. Earnings climbed significantly, he reported, exhibiting a gain of 80% over earnings per common share for the comparable 1958 quarter. Consolidated sales for the first quarter were \$13,637,000. Sales for the comparable quarter of 1958 were \$10,943,000. New income after taxes for the first quarter 1959 totalled \$642,000, compared with \$406,000 for the first quarter 1958, or 27¢ a common share in 1959 compared with 15¢ a share in 1958.

Reheis Acquires Tech-Chemical Corp.

Reheis Company, Inc., producers of aluminum salts for the cosmetic and pharmaceutical industries, announced the purchase of Tech-Chemical Corp., producer of liver preparations and other biologicals. According to president Daniel H. Reheis, the stock-cash transaction gives his firm possession of all Tech-Chemical operations, including its Stamford, Conn., headquarters and refining plant, and its Montevideo, Uruguay, bulk processing plant. Tech-Chemical president Robert W. Wilson, Jr. will become a vice-president and member of the Reheis board, it was reported.

"Acquisition of Tech-Chemical is another step in the direction of broad diversification and expansion that management initiated here last year," Mr. Reheis explained at the contract signing. He indicated that because products of the two firms have similar market patterns, the Tech-Chemical operation is

expected to fit perfectly into the Reheis organization.

Questioned on how the sale would affect labor status in Tech-Chemical's two branches, Mr. Reheis commented, "Except for Mr. Wilson's new position, the only change we will make will be the assignment of our assistant production manager, James Kosich, to the Stamford plant as project engineer."

Glass Container Shipments Reach New Peak

Glass container shipments in the first quarter of 1959 reached a new all-time high for first quarter shipments according to figures released in April by the Glass Container Manufacturers Institute, Inc.

Domestic shipments of new glass containers by 39 U. S. glass container manufacturers who are members of GCMI, and represent more than 92% of the industry, set a new record with an increase of 2.6 per cent over the units shipped the first quarter of 1958.

Dr. Paul Jewel Honored in California


The Society of Cosmetic Chemists, California Section, honored Dr. Paul Jewel, chief chemist of Max Factor & Co., as the founder and first chairman of the local chapter. Emory Smith, present chairman of the Section, presented Dr. Jewel with a plaque at the Society's regular membership meeting in Los Angeles. He credited him with being instrumental in the founding of the local chapter and in chairmanship of the group through its initial year.

Dr. Jewel, who received his Ph.D. in biochemistry from the Medical School of the University of Southern California, has been with Max Factor for the past 25 years. He is a member of The American Chemical Society, a Fellow of the American Institute of Chemists, and a member of Rho Chi and Phi Lambda Upsilon. He is also a member of the Board of Directors of the California Cosmetic Association.

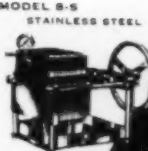
Two European Scientists Visit Colgate-Palmolive

Colgate-Palmolive Company's biological research laboratory on the New Brunswick, N. J. campus of Rutgers University was host last month to Professor Andre Simonart, a European specialist in skin research, and to Dr. Daniel Dresden, executive committee chairman of the Netherlands Organization for Industrial Research.


The visit by Dr. Simonart, head of the Pharmacology Department of Belgium's University of Louvain and director of the Institute of Experimental Therapy and Pharmacology at the university, was part of a tour of some of the leading scientific centers in the East. His trip to the United States was sponsored by the Armed Forces Research Command.



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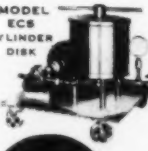
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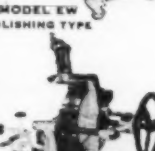
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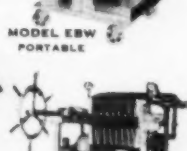
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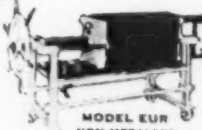
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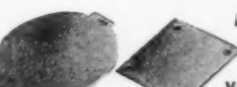
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Dr. Daniel Dresden (left), head of the Netherlands Organization for Industrial Research, is tested for radioactivity during a demonstration in the Colgate-Palmolive Company's Biological Research Laboratory at Rutgers University. Shown with the Dutch official are Dr. Joseph Brant (center), director of Colgate-Palmolive's Corporate Research, and Dr. Joseph Migliarese, head of the Biological Research Laboratory.



Prof. Andre Simonart (left, above), a leading European specialist in skin research, examines the result of an experiment during his tour of Colgate-Palmolive Company's Biological Research Laboratory on the New Brunswick, N. J. campus of Rutgers University. Shown with Dr. Simonart are Dr. Joseph Migliarese and Dr. Eugene Bernstein of the laboratory staff.

Dr. Simonart, who has written more than 100 publications, is an authority on thermal burns of the skin. In a seminar for the Colgate scientists he described his recent experiments in reactions to burns. Illustrating the talk with pictures and charts, he told of several approaches he and his assistants are taking to dis-

cover what causes auto-intoxication in severe burning.

Dr. Dresden's visit was part of a nation-wide tour undertaken to learn how American industries and research laboratories use radioisotopes. The Dutch scientist's U. S. trip will lay the groundwork for a new research program sched-

uled to be set up by the Organization for Industrial Research, which receives a 50-million dollar annual grant from the Dutch government and an equal amount from private industry.

Allied Chemical In Deal

The Allied Chemical Corporation announced in April the completion of negotiations for the purchase of Harmon Colors from the B. F. Goodrich Company. Harmon Colors, a producer of specialty organic pigments, is a part of the chemical division of B. F. Goodrich.

Thatcher Buys Plastic Tube & Bottle, Inc. Forms Plastic Container Div.

Formation of a Plastic Container Division was announced at the annual stockholders' meeting of Thatcher Glass Manufacturing Company, Inc. by its President, William J. Green. He stated that the new division was an outgrowth of the purchase by Thatcher of Plastic Tube and Bottle, Inc. of Nashua, New Hampshire.

Thatcher also recently announced the purchase of the assets and business of The Celon Company, Muscatine, Iowa, a major manufacturer of cellulose bands used as secondary seals for glass containers and also producer of a line of plastic closures.

Mr. Green cautioned that substantial research and development work remains to be done before the Plastic Container Division is in full production with a complete line of plastic tubes and bottles.

John H. Breck Elected Board Chairman of Brand Names Foundation

John H. Breck, Jr., executive vice president of John H. Breck, Inc., was elected chairman of the board of the Brand Names Foundation, Inc., at the

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annual members' day business meeting held at the Waldorf-Astoria Hotel on April 15. Breck previously served as chairman of the executive committee.

Edward R. Taylor, executive vice president, Motorola Inc., was called back as chairman of the Foundation's executive committee. From 1955 to 1957 Taylor served as chairman of the Foundation's board of directors. Since then he has been an honorary director, a status given to past chairmen of the board. His re-election marks the first time an honorary director has returned as an active board member.

Walter L. Jeffrey, vice president, American Motors Corp., was elected vice-chairman of the committee. **Frank Armour**, president of the H. J. Heinz Co., was elected vice chairman of the board of directors, and **Robert MacNeal**, president of the Curtis Publishing Co., was re-elected vice chairman.

Henry E. Abt was re-elected president of the Foundation. Abt has been president since 1947. Robert E. Connelly, vice president of Drexel Furniture Co., was re-elected treasurer.

Senator **John L. McClellan** of Arkansas and chairman of the Senate's Permanent Sub-Committee on Investigations, delivered the keynote address at the members banquet. To honor the celebration, Mayor Wagner, along with majors throughout the country, officially proclaimed April 12th to 19th as Brand Names Week.

Old Empire Acquires Space

Old Empire, Inc., Newark, New Jersey, has announced the acquisition of 15,000 sq. ft. of additional manufacturing and storage space. John DeElorza, president, stated that the expansion is designed to provide space for the company's new pharmaceutical area for packaging.

Hazel Bishop Expects Increased Sales

The highest volume of sales and profits in the company's history is expected for April, Robert G. Urban, president, told stockholders at the annual meeting of Hazel Bishop, Inc. last month. Shipments for the fiscal year ended Oct. 31, 1958 were \$11,209,112. The net loss was \$352,744 in contrast to a net loss of \$996,000 for the previous fiscal period. The company now has a tax loss carry-forward of \$1,500,000. Mr. Urban informed the stockholders that Hazel Bishop now is introducing two new products—eye makeup and refillable lipsticks—which the management expect to contribute to the company's sales, earnings and market position.

Manuel Rodas Of Myrurgia Opens Promotion Program

Manuel Rodas, general manager of Myrurgia, S. A. with headquarters in Barcelona, Spain, was honored at a cocktail reception held at the St. Regis Hotel on April 8th. Mr. Rodas and other principals in the Myrurgia organization were introduced to members of the press and



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Members of the Myrurgia staff at the reception at the St. Regis Hotel (left to right): Pablo Medina, general manager, New York; Manuel Rodes, general manager Myrurgia S.A.; E. Pando, member of the board of directors of Myrurgia; Louise Case, eastern sales representative; Albert Gleicher, administrative head in New York; Nelson King, New York sales manager.

to retail store personnel in the New York area. The cocktail party was followed by a special screening of the new film, "The Naked Maja", a Titanus production in technicolor starring Ava Gardner and Anthony Franciosa. Myrurgia and United Artists, who is releasing the film, have worked out a tie-in between Myrurgia's "Maja" fragrance and the movie, including displays, publicity, and theater exploitation during the opening of the picture in key cities throughout the United States.

Mr. Rodes, accompanied by his wife, visited the west coast and Mexico as well as New York. His primary purpose here was the reorganization of the Myrurgia sales and distribution operation.

Cosmetic Leaders At Anniversary Dinner

Four leaders of the cosmetics industry are officers of the 60th anniversary dinner of the National Jewish Hospital at Denver. Charles Revson, president of Revlon, Inc. is a co-chairman of the Manufacturers Committee for the dinner. Wellington Cross, vice president of Elizabeth Arden Sales Corp., Theodore Caro, of Chanel, and Richard Salomon, of Charles of the Ritz, are dinner vice chairmen.

The dinner was held May 13 at the Waldorf-Astoria Hotel in New York. The guest of honor was L. E. Oliver, vice president of Sears, Roebuck and Co. The event was for the benefit of the Denver institution, a non-sectarian medical center for free care and research in tuber-

culosis, asthma and other chest diseases and heart surgery.

60 Colleges Shared Pfizer Grants Of \$1.4 Million In 1958

Chas. Pfizer & Co., Inc. and the Pfizer Foundation have announced that grants for scientific research, medical education, health and welfare during 1958 amounted to approximately \$1.4 million.

More than 60 colleges and universities shared the grants which were made for advanced studies in medical, chemical and agricultural sciences. Investigations ranged from the effectiveness of a powerful new oral drug for treatment of diabetes to the administration of tranquilizers to beef cattle.

The 110-year-old pharmaceutical and chemical company earmarked \$236,000 for individual resident physicians, pharmacy internes and students to aid in the completion of their education.

The Pfizer grants covered a broad scientific frontier including long range nutritional studies among Haitian schoolchildren, 46 individual grants to graduating doctors from medical colleges in Japan for postgraduate studies, and a grant to the American University in Beirut for studies in infectious disease and parasitology chemotherapy.

Contributions of \$220,000 by the Pfizer Foundation benefited groups which support medical and pharmacy education, emergency and relief organizations, and health and philanthropic groups in communities where Pfizer has plants, offices and laboratories.

Book Reviews

INDUSTRIAL FATTY ACIDS AND THEIR APPLICATIONS. E. Scott Pattison, Editor. 230 pages. Hard covers. Reinhold Publishing Corporation, New York, 1959. \$7.00

This book covers the production and processing of fatty acids with emphasis on practical technology and the chemistry involved with it. The coverage also includes an up-to-date review of the chemistry, technology and applications of the derivatives having commercial importance. The book also reflects the growing industrial importance of fatty acids derived from tall oil—one of the most important recent advances. The fifty or more industries which use fatty acids will find here a wealth of dependable information on these important materials.

THE CHEMISTRY AND PHYSICS OF CLAYS. Alfred B. Searle and Rex W. Grimshaw. 944 pages. Hard covers. Interscience Publishers, Inc., New York, 1959. \$16.25

This is an entirely revised and enlarged edition of a very useful book for persons utilizing ceramics. In it are pertinent chapters dealing with the nature of clays and other ceramic materials; physical and structural properties of raw ceramic materials; chemical and physical changes in ceramic materials. The authors aver that ceramics, like other branches of science and technology, have advanced to an almost unbelievable degree. The increased knowledge of ceramic materials has led to a new technical science, a fact recognized by many universities and colleges which now include "ceramics" as part of their curriculum.

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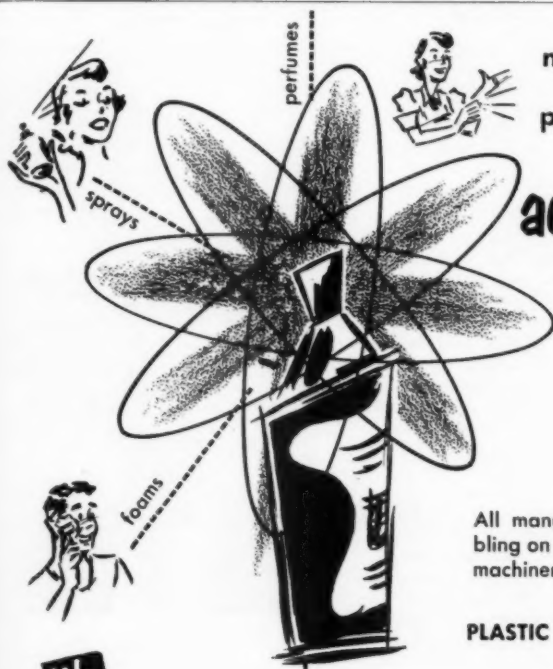
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PERSONALITIES

J. W. Dickinson, Jr. has been named general manager of Gillette Laboratories and **Dr. Daniel J. Johnstone** has been appointed medical director, announced the Gillette Company. Mr. Dickinson has been with Gillette Laboratories for the

Veronica L. Conley, secretary of the committee on cosmetics of the American Medical Association, was awarded a Ph.D. degree at the 281st convocation of the University of Chicago in March. Dr. Conley did her undergraduate work at

Robert T. Daily has been appointed manager of marketing for the Silicone Products Department, General Electric Company, by Jerome T. Coe, general manager. Mr. Daily succeeds Mr. Coe, former manager of marketing, who was named



J. W. Dickinson, Jr.



Veronica L. Conley



Robert T. Daily

past two years, serving as marketing director. Prior to that he was a supervisor in the brand department of the Toni Company. Dr. Johnstone was previously associated with the Warner-Lambert Research Institute and the Eli Lilly Co.

Boston University and holds Masters Degrees from Yale and the University of Chicago. She is listed in the recently published first edition of Who's Who of American Women.

department general manager in February of this year. Most recently serving as manager of rubber market development for the Silicone Products Department, Mr. Daily has been associated with G-E silicone operations since 1954. He has previously been sales manager for the department's western district.



Daniel J. Johnstone

Clark C. Sorensen has joined Hooker Chemical Corporation, Niagara Falls, N.Y., as director of public and personnel relations. Mr. Sorensen has previously held personnel managerial positions with B. F. Goodrich, Harris Intertype Corp., and American Machine and Foundry Company. He was a consultant to the Wage Stabilization Board in Washington during the Korean War, and is currently annual visiting lecturer on general management techniques and personnel administration at the Tuck School.

Albert B. Nichols Jr. has been appointed general sales manager of the Bradley-Sun division, American Can Company. Succeeding Mr. Nichols as assistant general sales manager is Harold M. Hansen, for 3 years Philadelphia district sales manager for the division and one of its predecessor companies, Bradley Container Corp.

Samuel C. Prusky has been named president of the Rexall Realty Corporation, according to Justin Dart, president of Rexall Drug Company. Mr. Prusky was formerly vice-president in charge of store operations of Owl Drug Company and then president of the Vitamin Corporation of America.



Arch Payne

Dr. Austin Smith, former editor of the AMA Journal, was appointed president of the Pharmaceutical Manufacturers Association, and president-elect **William Graham** became chairman of the board, at the Association's first annual meeting in Boca Raton, Florida. **Dr. Karl Rambeck** will continue as executive vice-president and **Dr. J. O'Neill Closs** will continue as administrative vice-president.

Arch Payne has been elected Assistant vice-president of Florasynth Laboratories, Inc., announced a spokesman for the company in New York. Mr. Payne is a veteran of over thirty years in this field and has been general sales manager of Florasynth Laboratories since 1947, a position which he will retain with his new duties and responsibilities.



Samuel B. Prussin

Samuel B. Prussin and Ethel F. Walsh were elected vice-presidents of Aerosol Techniques, Inc. Also appointed were David Benjamin as assistant to the president, and Val Rossetti as controller and financial officer. Mr. Prussin, who came to Aerosol Techniques from the Rexall Drug Company and Johnson & Johnson, was formerly director of new products and sales development. He will now direct all technical operations, including research and development, quality control and new products, and sales development. Mrs. Walsh, who has been director of sales services at Aerosol Techniques, was formerly with Bridgeport Brass Company, Connecticut Chemical Research Corp., and Propel Chemicals. She will supervise and co-ordinate production services, sales services and purchasing.



Ethel F. Walsh

Thomas W. Morningstar has been named general manager, and Mark P. Malkovich has been named sales manager of a new gum and technical products department of Morningstar-Paisley, Inc., according to Earl C. Lenz, vice-president. The new department consolidates the technical products and the water-soluble gum departments.

Charles E. Pressler has been named perfumer in their research laboratories by Rhodia, Inc., New Brunswick, N.J. Mr. Pressler has been engaged in the perfume industry for 20 years. He has held various positions in the laboratories of Naugatuck Aromatics Division of United States Rubber Co. and Colgate-Palmolive Co. For the past four years, prior to his association with Rhodia, Mr. Pressler was chief perfumer of Germaine Monteil Inc.

Oscar A. Mockridge, Jr. has been appointed sales manager of the New York office of Ertel Engineering Corp. Mr. Mockridge has had over fifteen years experience in pressure and vacuum filtration.

E. Lloyd Bernegger has been named president of the new Warner-Lambert Products Division which will handle the proprietary lines, including Listerine, Super Anahist and Bromo-Seltzer. George J. Abrams has been named president of the new Hudnut-DuBarry division, which will handle Richard Hudnut, DuBarry and Sportsman lines. J. S. Hewitt, who has headed up the family products division of Warner-Lambert, will remain as vice-president and consultant to the president on the company's advertised package goods throughout the world. Pierre de Tarnowsky, formerly with Mead Johnson, will be in charge of consumer products division.

Cornelius D. McGrath has been appointed field sales manager of the Atlas Powder Company's chemicals sales department, announced Edward J. Massaglia, vice president and general manager of the company's chemicals division. Theodore P. Malinowski, assistant director of the division's product development department, was named to succeed Mr. McGrath as manager of the industry group responsible for sales of Atlas chemicals to the cosmetic and pharmaceutical industries.

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Index **OF ADVERTISERS**

Abbe Engineering Co.	—	Gifford-Wood Co.	—	Polak's Frutal Works	14
Aerosol Techniques, Inc.	—	Givaudan-Delawanna, Inc.	43	Polak & Schwarz International, N. V.	—
Allied Chemical Corp., General	—	Goldschmidt Chemical Corp.	16	Polarome Manufacturing Company,	—
Chemical Division	4-5	Greff & Co., Inc., R. W.	—	Inc.	—
American Aromatics, Inc.	75	Halby Products	—	Reheis Co., Inc.	7
American Cholesterol Products,	—	Hazel Atlas Glass Division,	—	Rhodia, Inc.	—
Inc.	30, 32, 34, 36, 40	Continental Can Company	—	Richford Corp.	71
American Lanolin Corp.	—	Heine & Company	2	Risdon Manufacturing Co.,	—
Andersen, Carl N.	85	Heyden-Newport Chemical Corp.	—	The	Back Cover
Bertrand Freres	6	Hoffman-LaRoche, Inc.	—	Ritter & Co., F.	83
Bios Laboratories, Inc.	76	International Flavors & Fragrances,	—	Rona Laboratories, Inc.	—
Boake, Roberts & Co., Ltd., A.	—	Inc.	12-13	Rose Oil Products Co.	45
Bopf-Whittam Corp.	—	Ising Corporation, C. E.	—	Roure-Dupont, Inc.	—
Cameo Die & Label Co.	84	Katz & Co., Dr. Alexander, Div. of	—	Schimmel & Co., Inc.	—
Camilli, Albert & LaLoue, Inc.	86	F. Ritter & Co.	83	Scovill Mfg. Co.	—
Carr-Lowrey Glass Co.	18	Kenbury Glass Works	85	Shulton, Inc.	26
Cavalla, Inc., A.	84	Kessler Chemical Co., Inc.	78	Snell, Foster D.	85
Charabot & Co., Inc.	—	Knapp Products, Inc.	79	Stepan Chemical Co.	—
Chauvet & Co., Pierre	—	Kohnstamm & Company, Inc.	—	Stower & Oakley Ltd.	85
Chemo-Puro Mfg. Corp.	49	Lanaetex Products Inc., The	81	Sun-Lac, Inc.	—
Chiris Co., Antoine	—	Lanitis Bros., Ltd. .. Inside Back Cover	—	Synsieur Scientific Labs, Inc.	47
CIBA Company, Inc.	—	Lautier Fils, Inc.	—	Thomasson of Pa., Inc.	80
Citrus & Allied Essential Oils Co.	81	Leberco Laboratories	85	Tombarel Products Corp.	17
Classified Advertisements	85	Leonhard Wax Co., T.	84	Ungerer & Co.	—
Continental Can Company, Hazel	—	Lueders & Co., George	—	Universal Outlet	84
Atlas Glass Division	—	Martinat, Jean Jacques, Dr.	85	Van Amerigen-Haebler, A Division	—
Continental Filling Corp.	80	Maryland Glass Corp.	39	of International Flavors &	—
Croda, Inc.	—	Mauer-Wirtz	—	Fragrances, Inc.	12-13
Descollonges, Inc.	84	Monsanto Chemical Company	—	Vanderbilt Co., R. T.	—
Deutsche Hydrierwerke, G.m.b.H.	—	Naarden	—	Van Dyk Company, Inc.	—
Dodge & Olcott, Inc.	8	North Broad Labs.	85	Vanton Pump and Equipment	—
Dragoco, Inc.	68-69	Old Empire, Inc.	81	Corporation—A Division of	—
Emulsol Chemical Corporation	—	Owens-Illinois Glass Co.	—	Cooper Alloy Corporation	—
Ertel Engineering Corp.	77	Inside Front Cover	—	Verley & Company, Albert	—
Esperis, s.a.	—	Parento, Inc., Compagnie	1	Verona Aromatics, A Division of	—
Fairmount Chemical Co., Inc.	84	Parsons-Plymouth, M. W.	—	Verona-Pharma Chemical Corp. ..	11
Felton Chemical Co., Inc.	—	Peerless Tube Company	—	Webb & Co., Inc., R. D.	76
Fifth Avenue Protective Assoc.	84	Penick & Co., S. B.	—	White Metal Manufacturing	—
Firmenich & Co. Insert	65			Company	—
Foilcraft Printing Corporation	—			Whittaker, Clark & Daniels	83
Fritzsche Brothers, Inc.	—			Will & Baumer Candle Co., Inc.	76



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